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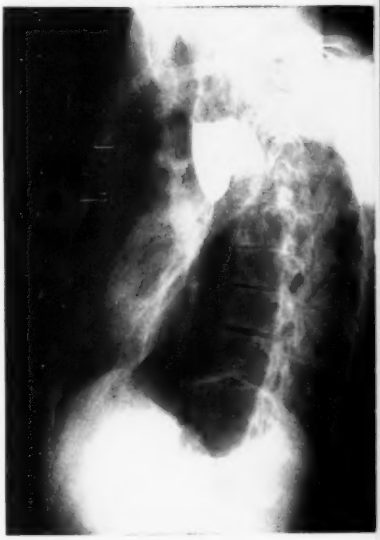

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Also the Official Publication of the Central Surgical Association and the Western Surgical Association

VOLUME 73 — NOVEMBER 1956 — NUMBER 5

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Published monthly by the AMERICAN MEDICAL ASSOCIATION. Editorial and Circulation Offices: 535 North Dearborn Street, Chicago 10, Illinois. Publication Office: Thompson Lane, Box 539, Nashville 1, Tennessee. Change of Address: Notice to the circulation office should state whether or not change is permanent and should include the old address. Six weeks' notice is required to effect a change of address. Second-class mail privileges authorized at Nashville, Tenn., Aug. 6, 1956.

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The Journal of the American Medical Association. Weekly. Annual Subscription Price: Domestic, $15.00 Canadian, $17.00. Foreign, $21.50. Price to students, interns, and residents: $9.00 in U. S. & possessions.

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A.M.A. Archives OF SURGERY

Gastric Carcinoma in Identical Twin Women

GEORGE A. SPIKES, M.D.
WILLIAM H. YATES, M.D.
HERBERT G. LIBERTY, M.D.
and
HARVEY RENGER, M.D., Hallettsville, Texas

Gastric carcinoma occurring simultaneously in monozygotic twins has been reported only three times. Two pairs of twins with cancer of the stomach were reported by Macklin [1] from the European literature, while Militzer [2] reported the only cases in the American literature in 1935.

We have had the opportunity to study an interesting pair of monozygotic twins in whom cancer of the stomach was apparently present simultaneously, although symptoms began and deaths occurred nearly a year apart. As will be shown, the cancers were not identical, histologically, but both were adenocarcinomas arising in the gastric mucosa. Every effort was made to determine the zygosity of these women, since there is no reported case known to us of gastric carcinoma occurring simultaneously in dizygotic twins. These women were considered monozygotic on the basis of their statements that they were often confused even by members of their own family, that their thinking and personalities were nearly identical, even though one married and the other did not. Their blood types were the same. Their heights and weights were almost identical. Their pictures as young women can hardly be told apart (Figure). women are practically indistinguishable (Figure). Coloring of the hair and eyes and general configuration of the face, ears, hands, and feet were the same. The following case histories will be of interest to geneticists as well as to surgeons, internists, and radiologists.

Submitted for publication April 26, 1956.
From the Renger Clinic.

Report of Cases

TWIN 1.—A 66-year-old white woman was first seen at the Renger Clinic on July 29, 1954, with complaints of anorexia for seven months and stomach and back pains, belching, and 10 lb. weight loss in the preceding seven or eight weeks. She had had a "nervous stomach" from about 1914-1927 and several years later had had epigastric pain which kept her awake at night but was relieved by milk and alkali. There was no history of jaundice or bleeding from the gastrointestinal tract.

On physical examination she was well nourished and in no acute distress. The blood pressure was 160/70 mm. of Hg, the pulse 66 per minute, and the temperature, 98.6 F. The head and neck were normal for her age. The chest was normal. The heart was not enlarged, but there were occasional premature ventricular contractions. There was a Grade 2 aortic systolic murmur. The abdomen was soft and flat. The sharp liver edge was palpable at the costal margin. There was a mass in the midleft upper quadrant, projecting 2 cm. below the costal margin in the midclavicular line. It was hard, movable, and slightly tender. The vagina was atrophic. There was a small cervical polyp, but the fundus and adnexal regions were normal. There was a urethral stricture with a caruncle. The extremities were normal.

A urinalysis showed a specific gravity of 1.025 and 20 red cells per high-power field. Flouroscopy the following day revealed a 4-5 cm. calcified

Photograph of the twins as young women.

density in the left subapex posteriorly, thought to be a tuberculoma and not a metastasis. The esophagus was normal. The stomach showed marked irregularity of both margins, extending from the pylorus to the fundus. This area was fixed, inflexible, and tender, and no peristalsis passed through it. Several films showed the constancy of the defect, which had the appearance of a submucosal, infiltrating carcinoma. The duodenal bulb was normal. On the medial aspect of the duodenal loop, a small 1.5 cm. diverticulum was seen. A Graham-Cole test produced very faint gall bladder visualization, but no stones were seen.

On Aug. 10, 1954, an exploratory laparotomy was performed. The uterus and ovaries were small and atrophic. On the inferior surface of the left lobe of the liver was a small palpable 2 cm. nodule, thought by the surgeon to be either a cyst or a hemangioma. The gall bladder was normal. An extensive neoplastic mass involved the distal two-thirds of the stomach. There were palpable nodes along the greater curvature and in the gastrohepatic ligament. The mass extended posteriorly and involved the pancreas, the transverse colon, and the mesocolon. A large lymph node from the greater curvature was removed for pathological study, which on cut and frozen section was thought to represent lymphosarcoma metastatic from the stomach. The lesion was not resectible, and the abdomen was closed.

Microscopic Examination.—The lymph node was almost completely replaced by a very cellular tumor, but a few foci of small lymphocytes remained. The tumor cells for the most part had distinct cytoplasmic borders and scanty cytoplasm which was pink and faintly granular but occasionally foamy. The nuclear membranes were sharp; many showed prominent nucleoli. Only a few mitotic figures were present. The cells were arranged in banks and cords which were supported by very thin strands of fibrocollagenous connective tissue. Because of the sharply defined cytoplasmic borders, which gave the cells an appearance of cohesiveness and the round sharply defined nuclei, the tumor cells were thought to be epithelial rather than lymphomatous. Mucicarmine stained sections revealed intercellular droplets of pink-staining material and confirmed the impression of the epithelial origin of the tumor cells.

Microscopic Diagnosis.—Lymph node, mesentery, secondary highly anaplastic carcinoma, metastatic from stomach.

The patient did well following surgery and received 1300 r measured in air through anterior and posterior epigastric portals between Aug. 18 and Sept. 4, 1954. This therapy resulted in marked reduction in polypoid formation within the stomach but did not affect its motility or mobility. The patient returned home, where she died in December, 1954. No autopsy was done.

TWIN 2.—A 67-year-old white woman, the identical twin sister of Twin 1, was first seen at the Renger Clinic on Jan. 19, 1955. She had

chronic complaints of backache, headache, intermittent substernal pain, and pain in the right upper arm and left elbow, all related to work. She had lost 16 lb. in the preceding few months, but attributed this to worry and overwork incident to her sister's illness and death in December, 1954.

She specifically denied any gastrointestinal complaints and claimed a good appetite. Physical examination revealed only a mild systolic hypertension due to arteriosclerosis and a mild senile vaginitis. These were treated.

She was next seen May 24, 1955, with complaints of anorexia, postprandial fullness, and nausea and loss of another 6 lb. in the preceding month. She had had a "nervous stomach" intermittently for years, some mild hypertension, pleurisy, and nocturia for several years. There was no history of jaundice or bleeding from the gastrointestinal tract.

On physical examination she was well nourished and in no acute distress. The blood pressure was 160/70 mm. of Hg, the pulse, 72 per minute, and the temperature, 98.6 F. The head and neck were normal for her age. The chest was normal. The heart was not enlarged, the rate and rhythm were regular, and there was a Grade 1 systolic mitral murmur. The abdomen was soft and flat. The liver and spleen were not palpable. No tumor mass could be felt. The vagina, cervix, fundus, and adnexa were normal for her age. There was no peripheral edema.

Flouroscopy on May 24, 1955, showed a normal chest, with only some aortic and hilar calcification. The esophagus was normal. The stomach was slightly constricted at its midportion and the mucosal pattern was interrupted. It was only slightly rigid below the fundus. Reexamination on May 31, 1955, revealed the same basic appearance, with failure to dilate in the midportion. The duodenal bulb and loop were normal.

On June 16, 1955, an exploratory laparotomy was done. There was an extensive neoplasm infiltrating through the anterior wall of the stomach. There were widespread metastases in lymph nodes of the transverse mesocolon, the gastrohepatic ligament, and the lesser omentum. There were other metastases to the liver and the mesentery of the small intestine. Nodes from the greater omentum, the liver, and a wedge from the anterior stomach wall were removed for pathological study. The lesion was not resectible, and the abdomen was closed.

Microscopic Examination.—The wedge from the stomach wall consisted of fibrocollagenous connective tissue in which there was malignant neoplastic growth represented by epithelial-like cells forming irregular glandular structures. Most of the cells were tall columnar in appearance, but some were flattened. The glands formed were of varying sizes. In some cases the cells were arranged in a papillary pattern. Scattered throughout the fibrous connective tissues were isolated individual malignant neoplastic cells, many of which had a signet-ring appearance. Sections from the omental node and the metastasis from the liver showed a similar appearance.

Microscopic Diagnosis.—(1) Stomach wall, adenocarcinoma of stomach. (2) Omentum, secondary adenocarcinoma metastatic from stomach. (3) Liver, secondary adenocarcinoma metastatic from stomach.

The patient recovered from surgery without complication. She had considerable pain in the left upper quadrant but no vomiting. In October, 1955, she had a stroke which caused a right hemiparesis and global aphasia. Her stools became tarry, she had another stroke in November, and she died in December, nearly a year after the death of her sister. No autopsy was done.

Comment

It seems doubtful that earlier diagnosis or suspicion of carcinoma in the second twin could have altered the outcome. It has been stressed [3] that tumors in identical twins occur at more nearly the same time, more often in the same place and with more certainty than in nonidentical twins. It is by reason of this simultaneous occurrence that this knowledge will be of little help in treatment of gastric carcinoma, since by the time it is diagnosible it is often incurable. Carcinoma of the stomach is undoubtedly prevalent in some families. We are, therefore, following a brother of these twins with semiannual flouroscopy.

Gastric carcinoma may reasonably be estimated to cause 50,000 deaths per year.[4] In this country, according to Anderson,[5] 1 in 45 newborn infants is a twin, and between one-quarter and one-third of these are uniovular, so that approximately 1 person in 150 is an identical twin. Therefore, if one assumes 50,000 gastric carcinoma deaths per year, and if there are no determinants save chance, over 300 identical twins should die in this country annually from gastric carcinoma. If gastric carcinomas are always genetically determined in identical twins, then there must be over 300 "pairs" of identical twins dying in this country annually from this disease. As noted above, the sub-

jects of this report are the second pair of identical twins dying of carcinoma of the stomach reported in this country. The first pair was reported by Militzer,[2] in 1935. Assuming again inevitable genetic determination, there were over 6000 pairs of identical twins dead of gastric cancer before the second pair is reported now, over 20 years later.

Macklin,[1] in 1941, reported from the European literature two pairs of identical twins in which only one of each pair developed carcinoma, while the other twin was unaffected for 16 and 7 years, respectively. When one considers the drama of having a pair of identical twins affected with gastric carcinoma as opposed to the nearly everyday occurrence of individual cancers, it is not unusual to expect that similar and simultaneous cancers affecting both of identical twins would be reported much more frequently. At any rate these considerations make us less prone to be dogmatic about the subject than are some other authors * who state that there is no reported case of a tumor affecting one of homologous twins without the other also being affected and suggest that while a general predisposition might lead to tumors in each of a pair of twins, it could not explain their identical location or simultaneous occurrence. Much light could be shed on this subject if there were more reports of cancers in identical twins.

* References 6 and 7.

Summary

The fourth reported pair of gastric carcinomas in identical twins is presented in detail along with the evidence for the monozygosity of the twins and detailed pathologic reports on the biopsy specimens. Statistical and other evidence is presented to temper the older idea that monozygous twins must necessarily have simultaneous identical tumors, and a plea is made for better, more complete reporting of tumors in twins.

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Dissecting Aneurysm of the Renal Artery

RUTHERFORD S. GILFILLAN, M.D.
WILLIAM R. SMART, M.D.
and
WARREN L. BOSTICK, M.D., San Francisco

The vast majority of dissecting aneurysms originate in the aorta, with the main branches involved only by extension from the aortic source. Edwards, however, expressed the opinion that local dissecting aneurysm superimposed on atheromatous changes may be associated with thrombosis of peripheral arteries and cites a case of local dissection in the popliteal artery.[1] Lovitt and Corzine also report the occurrence of dissecting aneurysm in the coronary arteries.[2] Most dissecting aneurysms are found in relation to atherosclerotic or medial necrotic vascular changes. Careful perusal of the literature failed to reveal a case of local dissection of the renal artery without evidence of aortic involvement.

Report of a Case

A 47-year-old man was in apparent good health until eight hours prior to hospitalization (April 26, 1952), at which time there was the sudden onset of deep, nauseating, nonradiating, intense left flank pain. A moderate degree of shock was present when first seen by his family physician, and a tentative diagnosis of left ureteral calculus was made. An episode of left flank pain six years previous had been attributed to ureteral calculus.

On admission to the hospital he was acutely ill, with absence of peristalsis, abdominal distention, nauseas, and vomiting. The left flank was tender on palpation. Urinalysis showed a specific gravity of 1.026; albumin and sugar were negative, acid reaction. The sediment contained 3-4 white blood cells per high power field, which could have been secondary to an existing prostatitis. The leukocyte blood cell count was 12,550, with a normal differential count showing 87% polymorphonuclear cells. At the time of admission he was afebrile, and his brachial blood pressure was 132/82 mm. of Hg. The nonprotein nitrogen was 48%, creatin, 4.2%.

An excretory pyelogram failed to demonstrate evidence of a ureteral stone. There was poor dye concentration in the right side and no demonstrable function on the left. A phenolsulfonphthalein test showed a total of 40% dye recovered in two hours. Retrograde study demonstrated no function on the left side, despite a retrograde pyelogram visualizing a normal left ureter and renal pelvis. The right kidney showed 25% phenolsulfonphthalein in 15 minutes and a normal pyelogram. A diagnosis of left renal arterial occlusion was made.

During the next seven days there was slow recovery from the shock of the acute vascular episode, and the intense adynamic ilius subsided. During this period daily observation of the urine was carried out, which showed microscopic blood in all samples. On the fourth day following his attack dark brown urine was passed, which microscopically showed white cells, red cells, cellular debris, and casts of all types. During the ensuing four days the urine cleared grossly and remained so. The patient was discharged from the hospital on the eighth day of his sickness. The nonprotein nitrogen had dropped to 37% and the creatine to 2.4%. On the day of discharge an excretory pyelogram again showed no function on the left side. Four days following discharge from the hospital the blood pressure gradually rose from 130/80 to 195/120 mm. of Hg. During this period he showed the first clinical signs and symptoms of an acute hypertension, with headaches, anxiety, fatigue, and insomnia, as well as skin pallor and hyperhydrosis. The patient's entire personality seemed to be changing.

Twelve days following the initial episode an aortogram was done under general anesthesia which showed an essentially normal aorta with both renal arteries markedly sclerotic and the left one blocked approximately 2 cm. from the aorta (Fig. 1, *A* **and** *B*). At the time of the aortogram his blood pressure was recorded as 198/112 mm. of Hg.

Received for publication April 27, 1956.

Clinical Instructor in Surgery (Dr. Gilfillan); Clinical Instructor in Urology (Dr. Smart), and Associate Professor of Pathology (Dr. Bostick), University of California School of Medicine.

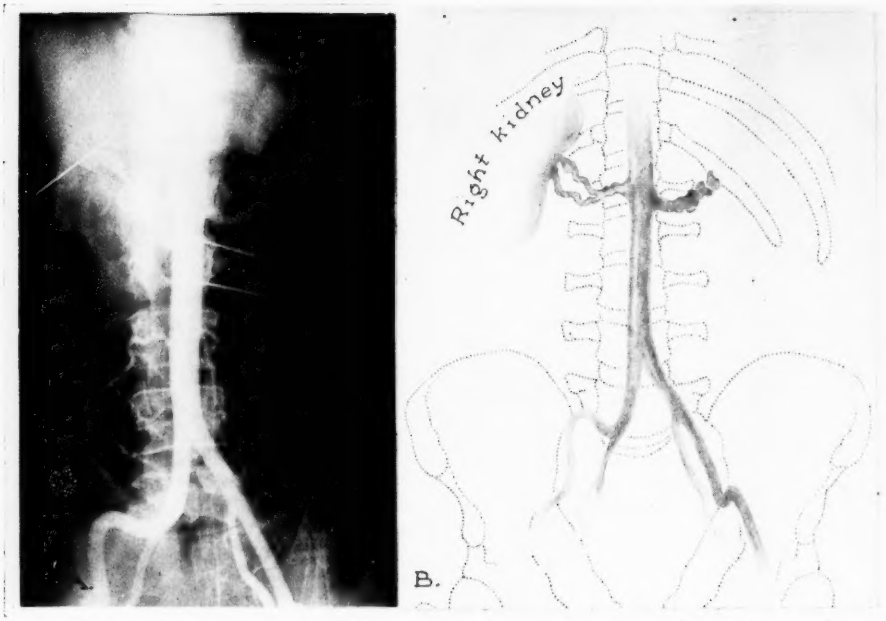

Fig. 1.—Translumbar aortogram (May 7, 1952) demonstrating obstruction of left renal artery and arteriosclerotic changes in both renal arteries, with minimal changes in the aorta and iliac arteries. *A*, Film 2. *B*, composite drawing.

Left nephrectomy was performed on May 8, 1952, revealing a kidney with multiple ischemic infarcts. The renal artery was found to be dilated, and the first pedicle clamp applied cut through the friable arterial wall. A small aberrant artery was present, entering the upper pole of the kidney. A local dissection of the renal artery with superimposed thrombosis was the underlying pathology. The dissection started about 1.5 to 2 cm. from the aorta and extended to the kidney. The absence of demonstrable aortic disease with maximal renal artery changes is significant. The upper pole independent arterial pathway may account for the observed hypertension.

Pathological examination revealed a capsule which stripped with ease. There were large mottled discolorations scattered over the surface of the kidney, consisting of large areas of ischemic infarction measuring as much as 2.0 cm. in diameter with surrounding zones of hemorrhage measuring 0.5 cm. in breadth. At the pelvis the renal artery showed what appeared to be a dissection between the coats of the artery filled with blood, with the result that there was a tiny compressed lumen which contained a thrombus which extended throughout the length of the renal artery and into one or two of the smaller primary branches of this artery. The noninfarcted portion of the kidney consisted chiefly of tissue near the upper pole and showed a cortex which measured 0.5 cm. in thickness, with distinct corticomedullary markings. The pelvis showed hemorrhagic mucosa which extended down the entire length of the ureter.

Microscopic examination revealed ischemic infarction throughout the renal parenchyma. The areas of infarction were confined almost exclusively to the cortical zone, the medullary structures being somewhat edematous and showing moderate chronic inflammatory reaction. The blood vessels were quite remarkable, particularly the larger arteries. In the renal artery there was definite arteriosclerotic alteration with several initimal plaques and some medial degenerative changes. This was accompanied by extensive hemorrhages into the plaques, causing a true dissecting aneurysm between the media and advential zone (Fig. 2 *C*) extending for a long length of the artery with compression of the lumen of the artery into a small cleft (Fig. 2 *A*). A mild, subacute inflammatory reaction was present within the walls of the artery, accompanied by early fibroblastic response. Proliferation or extension of the mural hemorrhage extended along several of the primary branches of the renal artery.

Final pathological diagnosis was renal arterios-

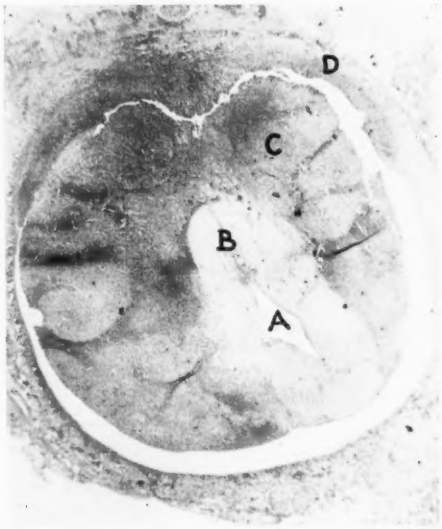

Fig. 2.—Cross section of the dissecting aneurysm of the left renal artery (May 8, 1952). *A*, lumen. *B*, media compressed and collapsed. *C*, dissecting blood mass. *D*, adventitia.

clerosis with extensive intramural hemorrhage and dissection of the renal artery and the main branches accompanied by multiple renal infarcts.

The sclerotic process in the right renal artery forces a guarded prognosis.

Comment

The case presented is that of an arteriosclerotic dissecting aneurysm of the renal artery not involving the abdominal aorta. Angiography visualized an aorta remarkably free of arteriosclerosis and showing only the early changes of tortuosity in the iliac vessels. Figure 3 shows the data relative to the hypertension and is presented because of the recent interest in renal infarction or ischemia as a cause of hypertension, substantiating Goldblatt's data on the production of hypertension in dogs by reduced blood flow through the renal arteries.[3] Cornwell[4] reported a case of hypertension due to partial renal vascular occlusion apparently without infarction, and Freeman and co-workers, a similar case in 1954.[5] The latter case was of unusual interest in that a thromboendarterectomy of the renal artery led to a recovery from the hypertension, as did removal of the kidney in this case.

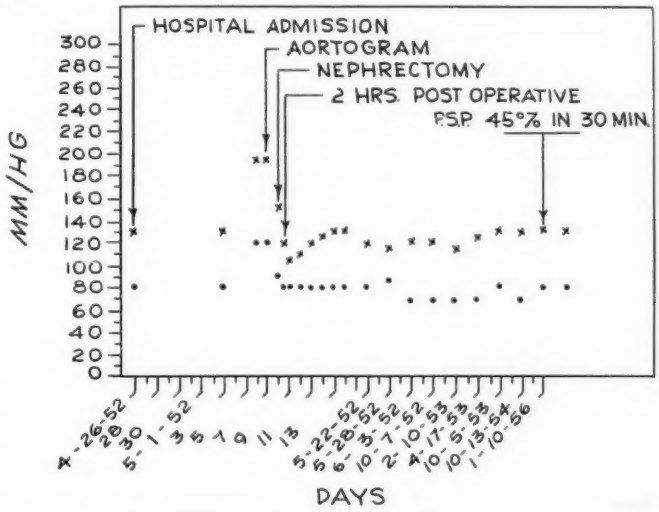

Fig. 3.—Blood pressures right arm supine 1952-1956.

Following nephrectomy the blood pressure dropped to 120/70 and has remained well within normal limits. The last observation was Jan. 10, 1956, at which time the pressure was 130/80. The phenolsulfonphthalein test is now 45% in 30 minutes. The patient is in good health and feels well.

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Unsuspected Lesions in Anal Tissue Removed for Minor Conditions

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The examination of tissue removed in the course of "minor" surgical procedures frequently consists of a cursory gross inspection, if there is any examination at all. There is no agreement regarding the proper disposal of tissue removed in the operating room. In general, it is recommended that "all tissues removed at operation shall be sent immediately to the clinical laboratory to be examined and reported upon by the pathologist." [1] No mention is made of the extent of the examination, or whether the examination is to be both gross and microscopic. Legally, even this minimum standard does not appear to be necessary. In the *Legal Guide for American Hospitals,* the statement is made that "all tissues removed in the operating room should be examined, described and diagnosed by a competent pathologist, excepting tissues such as tonsils and teeth, in which the pathologic changes are quite obvious." [2] It is not clear whether the excepted tissues, such as tonsils and teeth, should not be examined, described, and diagnosed; or whether they should be examined, described, and diagnosed, but not by a competent pathologist.

In the revision of the essentials of an approved internship by the American Medical Association, attention is directed to the duties of the pathologist, one of which is "to examine or supervise the examination of all tissues removed in surgical operations." [3] Again, there is no indication of what is considered an adequate examination. MacEachern [4] specifically states, however, that whether a pathologist makes a diagnosis from the gross specimen or by microscopic examination of the tissue is left entirely to his discretion.

Many pathologists do not bother to examine microscopically such innocent and minor surgical specimens as tonsils, hernial sacs, hemorrhoids, etc. Although few examinations of these specimens will dramatically disclose findings of major importance, yet such findings do occur frequently enough to warrant complete examination.

To emphasize the importance of this matter, the records of the Veterans Administration Hospital, Bronx, N.Y., were searched for data on patients who had been operated on for minor conditions of the anus since 1947. Every specimen removed was examined grossly and microscopically. There were 1470 operations for hemorrhoids, 180 for fistula in ano, and 240 for fissure in ano and other miscellaneous minor conditions. These totaled 1890 such operations. On microscopic examination of tissues excised at these operations, other unexpected lesions were discovered in 21 cases (1.1%) distributed as shown in the Table.

Summary of Lesions

Lesion		No. of Cases
Carcinoma in situ		5
Squamous-cell carcinoma		7
Myoblastoma		1
Schistosomiasis		3
Nevi		3
Intradermal nevus	1	
Junctional nevus	1	
Compound nevus	1	
Melanocarcinoma		1
Tuberculosis		1
Total		21

Submitted for publication Feb. 15, 1956.

From the Laboratory Service, Veterans Administration Hospital.

Report of Cases

CASE 1.—A 32-year-old Negro man presented a six-month history of constipation, rectal bleeding, and weight loss. A hemorrhoidectomy was performed. Microscopic examination of the excised tissue showed epidermoid carcinoma in situ of the anal mucosa.

CASE 2.—A 32-year-old white man presented a history of right orchiectomy for seminoma, followed by radical lymph-node dissection and x-radiation four years previously. He was operated upon for hemorrhoids, and a carcinoma in situ of the anus was reported (Fig. 1). This lesion was further treated by local excision and apparently healed. There has been no recurrence of the anal lesion.

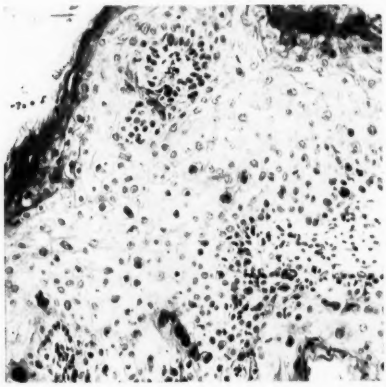

Fig. 1 (Case 2).—Photomicrograph showing epidermoid carcinoma in situ, × 90.

CASE 3.—A 52-year-old white man complained of "tightness" in the anus and "narrow" stool for about 10 years. There had been no pain, no loss of weight, and no progression of symptoms for the last two years. Examination disclosed a stricture of the anal canal and rectum, which was excised by an abdominoperineal resection. Microscopic examination of the excised tissue disclosed an intraepidermoid carcinoma superimposed on lymphogranuloma venereum. The patient has remained well.

CASE 4.—A 47-year-old white man had a hemorrhoidectomy performed because of occasional bleeding. Carcinoma in situ of the anal mucosa was found, in addition to the hemorrhoids.

CASE 5.—A 62-year-old white man complained of occasional rectal bleeding and prolapse of hemorrhoids. Examination disclosed internal and external hemorrhoids and a small anorectal smooth sessile polyp. The hemorrhoids and the polyp were removed at the same time. The polyp was derived from rectal mucosa and showed marked atypia of the glandular epithelium, carcinoma in situ in an adenomatous polyp (Fig. 2).

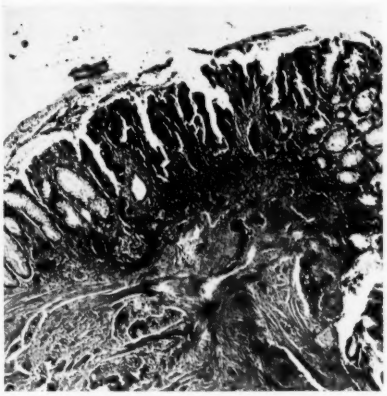

Fig. 2 (Case 5).—Photomicrograph showing carcinoma in situ in an adenomatous polyp, × 30.

CASE 6.—A 53-year-old white man complained of blood-stained rectal discharge for about 14 months. A diagnosis was made of "horseshoe fistula and condylomata." A biopsy of the fistula disclosed squamous-cell carcinoma. An abdominoperineal resection was performed, with the establishment of a permanent colostomy (Fig. 3).

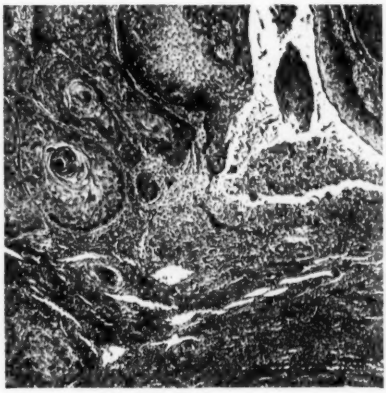

Fig. 3 (Case 6).—Photomicrograph showing squamous-cell carcinoma, × 30.

CASE 7.—A 32-year-old Negro man had a hemorrhoidectomy performed. Microscopic examination of the excised tissue disclosed a squamous-cell carcinoma, Grade 1. The original site of operation was widely excised, and only a small focus of intraepidermal carcinoma was found. The wound healed.

CASE 8.—A 52-year-old white man had pruritus

ani for 30 years and hemorrhoids for 5 years. A hemorrhoidectomy was performed, and microscopic examination of the excised tissue disclosed an epidermoid carcinoma (Fig. 4). Further treatment consisted of an abdominoperineal resection

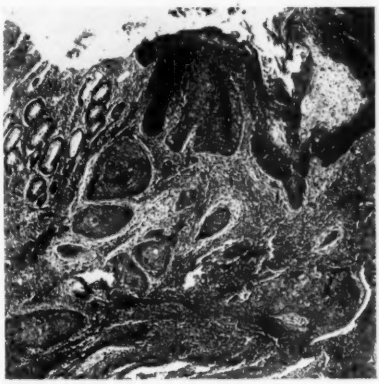

Fig. 4 (Case 8).—Photomicrograph showing infiltrating epidermoid carcinoma, × 30.

of the anus and rectum, with bilateral inguinal-node dissection. Examination of the specimen revealed squamous-cell carcinoma in the anus, but the lymph nodes showed no evidence of tumor.

CASE 9.—A 69-year-old white man had been treated in the hospital during six admissions, starting in 1940, for pulmonary tuberculosis, arteriosclerotic heart disease and myocardial fibrosis, and multiple draining rectal sinuses. A biopsy of rectal tissue made during the last stay in the hospital disclosed squamous-cell carcinoma (Fig. 5). Before surgical treatment could be undertaken, a thrombosis of the left femoral vein developed, following which the patient died.

Fig. 5 (Case 9).—Photomicrograph showing squamous-cell carcinoma. × 30.

Fig. 6 (Case 11).—Perianal fistulae, site of squamous-cell carcinoma.

CASE 10.—A 67-year-old white man had an asymptomatic lesion in the perineum, adjacent to the anus, which on microscopic examination revealed a squamous-cell carcinoma, Grade 1.

CASE 11.—A 24-year-old white man had multiple perianal fistulae which were excised. Microscopic examination disclosed squamous-cell carcinoma (Fig. 6).

CASE 12.—A 70-year-old white man had complained of rectal pain and bleeding for one year. A hemorrhoidectomy was performed. Microscopic examination of the excised tissue disclosed squamous-cell carcinoma (Fig. 7).

Fig. 7 (Case 12).—Photomicrograph showing infiltrating low-grade squamous-cell carcinoma, × 7.5.

CASE 13.—A 39-year-old Negro man was told of the presence of a perianal cyst when he was discharged from the Army in 1946. In 1949, he noted a "boil" at this site which ruptured and

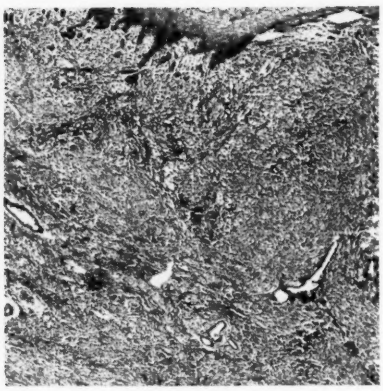

Fig. 8 (Case 13).—Photomicrograph showing benign myoblastoma. Note characteristic pseudoepitheliomatous hyperplasia of overlying epithelium, × 30.

drained pus. Hemorrhoids had been present for 18 years, with occasional bleeding. Physical examination disclosed a fistula in ano with an ulceration. A biopsy specimen was taken from the wall of the ulcer, and microscopic examination showed a benign myoblastoma. The entire lesion was then excised (Fig. 8).

Case 14.—A 27-year-old white man complained of a bleeding hemorrhoid. Examination disclosed the source of the bleeding to be a hypertrophied anal papilla. The excised specimen, on microscopic examination, showed ova of Schistosoma mansoni (Fig. 9).

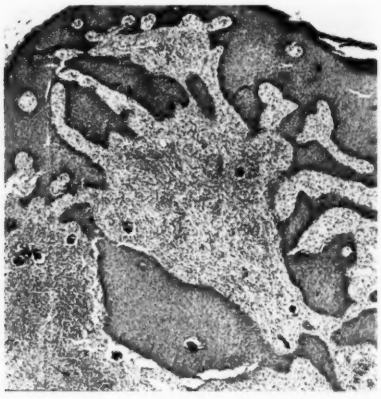

Fig. 9 (Case 14).—Photomicrograph showing hypertrophied anal papilla with multiple Schistosoma ova, × 30.

Case 15.—A 27-year-old white man complained of rectal pain and bleeding. Hemorrhoids and a fissure in ano were excised. Microscopic examination of the tissue showed external and internal hemorrhoids and multiple Schistosoma ova surrounded by foreign-body giant cells.

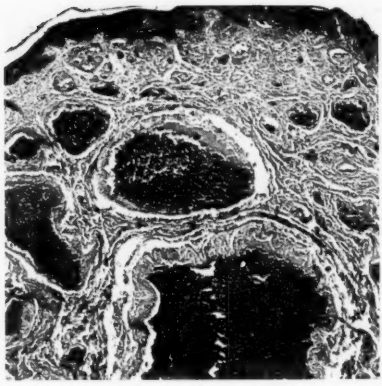

Fig. 10 (Case 17).—Photomicrograph showing external hemorrhoids and intradermal nevus, × 30.

Case 16.—A 28-year-old white man complained of pain on defecation. A small anal fistula and cryptitis were noted. The excised tissue revealed ova of Schistosoma mansoni.

Case 17.—A 30-year-old white man had a routine proctoscopic examination. Hemorrhoids and "papillomata" were discovered. Microscopic examination of the excised tissue showed external hemorrhoids and an intradermal nevus (Fig. 10).

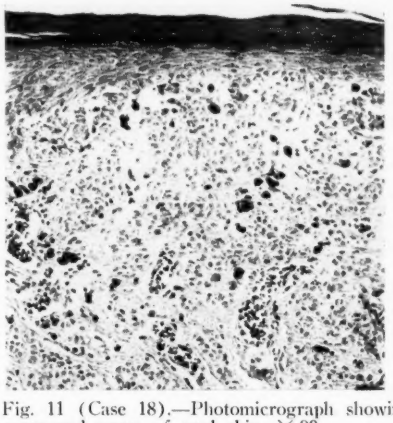

Fig. 11 (Case 18).—Photomicrograph showing a compound nevus of anal skin, × 90.

Case 18.—A 22-year-old white man had adjacent to the anus a small, dark, asymptomatic skin lesion, which was excised. Microscopic examination showed a compound nevus (Fig. 11).

Case 19.—A 33-year-old white man had an asymptomatic skin lesion of the anus. The lesion

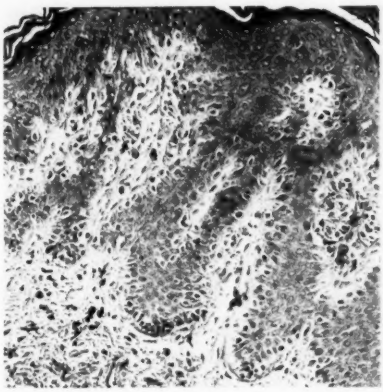

Fig. 12 (Case 19).—Photomicrograph showing a junctional nevus of anal skin, × 90.

was excised. Microscopic examination showed a junctional nevus (Fig. 12).

CASE 20.—A 25-year-old white man had a small fistula in ano which was excised. A small discolored lesion in the skin of the anus proved, on microscopic examination, to be a melanocarcinoma (Fig. 13). He was treated further by a bilateral radical groin dissection and has shown no evidence of recurrence.

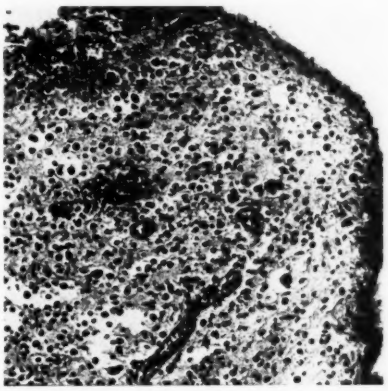

Fig. 13 (Case 20).—Photomicrograph showing melanoma of anal skin, × 90.

CASE 21.—A 32-year-old Negro man had a hemorrhoidectomy performed. Microscopic examination of the excised specimen disclosed histologic evidence of tuberculosis (Fig. 14). A roentgenogram of the chest then revealed a right apical infiltrate, which proved to be tuberculous.

Comment

The incidental discovery of premalignant or malignant lesions of the anus in the course of treatment for some benign conditions has been cited previously. In addition to instances of intraepidermal carcinoma of Bowen's type,* there have been impressive reports of epidermoid carcinoma of the anus superimposed on fistulas, hemorrhoids, fissures, lymphophathia venereum, and radiation injury. Binkley[7] reviewed 125 cases of epidermoid carcinoma of the anus and rectum. Of these, there were 32 cases in which the diagnosis of carcinoma had been completely overlooked: 8 patients were operated on for hemorrhoids; 7 received treatment other than surgery for hemorrhoids; 5 were treated for anal conditions with suppositories and ointments; 4 had operations for anal fissures; 1 was operated on for anal fistula, and 7 had miscellaneous anal surgery without any specific diagnoses.

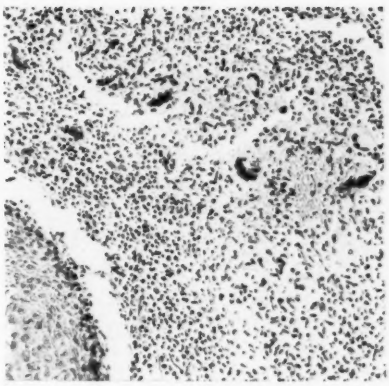

Fig. 14 (Case 21).—Photomicrograph showing epithelioid tubercules of the anus, × 90.

Similarly, Grinnell,[8] who analyzed 49 cases of squamous-cell carcinoma of the anus, cited such tumors arising in a stricture of lymphogranuloma venereum, anal fistula, and periurethral abscess.

The incidence of epidermoid carcinoma of the anus among malignant tumors of the terminal bowel (anus and rectum) has been reported† variably from 1.7% to 6%, an incidence frequent enough to warrant increased recognition of this area as a possible site of malignant tumor. In our own series, the incidence was 2.5%.

* References 5 and 6.

† References 9 and 10.

Although the anus is the commonest site of origin of melanoma in the intestinal tract, the total cases reported have not been much over 100.[11] It is interesting that the first reported instance of anal melanoma appeared as far back as 1857.[12] The anus was the primary site in about 1% of all melanomas reported at the Mayo Clinic.[12] Of these seven patients with anal melanoma, one was alive and well after 10 years. In the one case reported here, the patient has been found to be alive and free of evidence of recurrent or metastatic disease two and a half years after operation.

The incidental discovery of Schistosoma ova, or granulomata due to tuberculosis, or uncommon tumors as demonstrated here is an additional reward for careful examination of all surgical specimens.

Other lesions which one would have expected to encounter in such a series were conspicuously absent. These include (1) basal-cell carcinoma, (2) epidermoid carcinoma of the colon, and (3) sarcoma. Their occurrence, however, in this area is rare.[12]

Summary and Conclusion

Among a total of 1890 patients who were operated on for minor conditions of the anus, such as hemorrhoids, fissures, and fistulae, there were found 21 patients, or 1.1%, with more or less serious lesions which were discovered upon microscopic examination of the surgically removed tissue.

All tissue removed in the course of surgery for a benign lesion should be sent to the laboratory for microscopic examination. "Tissues that require excision also require microscopic examination"[13] is a slogan which, if followed, will bring adequate diagnostic rewards.

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Sucrose Space Determinations in Thermally Injured Animals

Evaluation with Use of the Lymphatic Cannulation Technique

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and
CAPT. JERROLD M. BECKER (MC), U.S.A.R.

Numerous studies of the profound fluid and electrolyte shifts following thermal injury have been carried out in order to determine the direction and magnitude of these changes. A better method of fluid therapy for extensively burned patients would follow a more thorough understanding of the basic physiologic changes following thermal injury.

Measurement of deuterium oxide is an accurate and fairly simple method for determining total body water.[1] There is no simple procedure, however, which is universally accepted to measure extracellular fluid content, although many ions and substances have been utilized.* This circumstance is most unfortunate, because not only are extracellular fluid compartment measurements important in themselves but intracellular water content is determined by subtracting the extracellular fluid content from the total body water.

In 1952, Young and Raisz [6] reported an anthrone procedure for determination of inulin in biologic fluids. This was extended to include sucrose, which has a more rapid diffusion rate because of its smaller molecular weight. Since 1952, sucrose has been used in this laboratory to measure extracellular fluid compartments.

Dogs were subjected to a 30% body-surface burn, and an average reduction of the sucrose space of 31.67% was found in each animal acting as its own control.[7] Clinically one would expect an expansion of the extracellular space at the expense of the intravascular and intracellular space compartments, because of the large accumulation of fluid in the burned area. This experiment was carried out to determine (1) if thermal trauma with edema formation in capillary injury hinders or prevents the entrance of sucrose into the burned area and (2) whether blood samples accurately reflect what is taking place in the extracellular fluid compartment in the normal and in the burned animal.

Materials and Method

Fourteen healthy adult mongrel dogs were used. There was a weight range of 12 to 20 kg. The animals were weighed three times a week until their weight had stabilized, which took as long as six weeks in some cases. Food was withheld from the animals for 12 hours prior to the experiments. Fluids were withheld for four hours prior to the experiment.

The dogs were anesthetized with pentobarbital (30 mg/kg.). One hind leg was clipped to the groin. A standard burn was produced by immersing this leg up to the groin in 90 C water for 20 seconds. The animals were then observed for eight hours, during which time no fluid therapy was given. Minimal amounts of pentobarbital were given to sedate the animals. At the end of eight hours the burned extremity was swollen and

Submitted for publication May 2, 1956.

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The Commanding Officer of the Unit, Lieut. Col. Curtis P. Artz (MC), gave continued support, encouragement, and advice throughout the time required for this experimental work. Sp. 3 Thomas H. Armao and Sp. 3 Albert Skuta gave valuable technical assistance.

* References 2-5.

edematous and provided an adequate means to study the movement of sucrose in the post-thermal injury state. The femoral vessels in the unburned limb were exposed through a small incision in the groin, and both the artery and vein were cannulated with polyethylene tubing. A lymphatic trunk in the burned ankle was cannulated in all of the animals, and 6 of the 14 animals also had a lymphatic trunk cannulated in the normal hind limb. This technique will be described elsewhere.[8]

A 10% solution of sucrose was injected into the femoral vein at a rate of 1 cc. per minute for 20 minutes. A Bowman pump was used to insure a constant rate of delivery. Simultaneous blood and lymph samples were taken every 15 minutes for 2 hours after the initiation of the sucrose infusion. Clotting posed no problem, and anticoagulants were used neither parenterally nor locally.

The anthrone method of Young and Raisz was used to determine the sucrose concentration in the blood and lymph samples. The optical densities were plotted on semilogarithmic paper. Volumes of distribution of sucrose in these thermally injured animals were not calculated, since previous experiments in this laboratory consistently gave a markedly decreased sucrose space. There is more water per cubic centimeter of lymph than there is in plasma because of the higher protein concentration in the plasma. Unless a correction is made, the concentration of sucrose in the lymph would be slightly higher. This correction was not made for the difference in protein content, since the main interest in this experiment was in rates rather than in absolute values.

Results and Comment

Complete recovery of sucrose in the urine of the dog is not possible.† Consequently it was necessary to compensate for urinary loss prior to equilibrium by an extrapolation technique. The formula used was

$$V=\frac{I}{P_o}$$

where

V=volume of distribution
I=amount injected
P_o=plasma concentration at time zero, implying instantaneous injection, distribution, and no renal loss.

By determining the disappearance rate after the slope had become linear, the concentration at time zero could be calculated by extrapolating a line which was fitted by the method of least squares (Fig. 1). This would take into consideration the amount of sucrose lost prior to equilibration. In using such a procedure, it must be assumed that the linearity of the disappearance rate

† References 9 and 10.

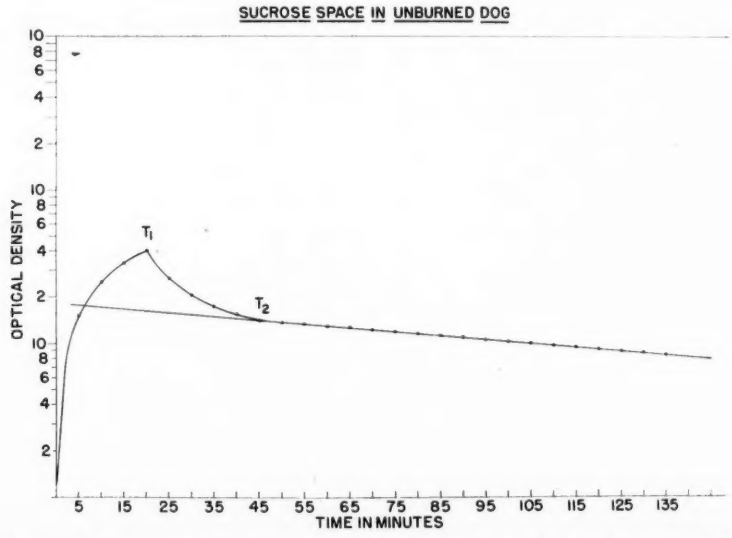

Fig. 1.—Sucrose space determination utilizing a 20-minute infusion plus extrapolation of disappearance curve.

after equilibrium had been achieved was the result of a single function, namely, renal loss. To test the validity of this assumption, sampling of extracellular fluid compartment was carried out by means of lymphatic cannulation.

When the optical densities of the blood samples are plotted on semilogarithmic paper, the sucrose concentration is found to rise rapidly during the 20-minute infusion. Thereafter the concentration drops rapidly in a curving fashion for approximately 30 to 40 minutes, at which time the disappearance curve becomes linear. During the period immediately following infusion, the sucrose is not only being excreted by the kidneys but is also diffusing into remoter areas of the body. Once the slope became linear, it was thought that renal excretion accounted for nearly all of the sucrose lost from the blood. If sucrose were still diffusing into remoter areas in any large quantity, the optical densities—when plotted on semilogarithmic paper—would continue to curve in a nonlinear fashion.

Six of the fourteen animals had lymphatic channels in both hind limbs cannulated. Lymph flow in the normal limb is notoriously slow, and lymph samples were obtained with some difficulty. In order to obtain adequate quantities of lymph over the two-hour period, vigorous massage and manipulation was necessary, particularly toward the end of the experiment. The results which are obtained under these circumstances are questionable because of these unphysiologic maneuvers.

After the initiation of the sucrose infusion the concentration of sucrose in the lymph from the normal limb rose rapidly for approximately 40 minutes. The concentration then began to decrease in an almost linear fashion. The blood and lymph sucrose concentrations were identical momentarily between 30 and 40 minutes after the start of the sucrose infusion (Fig. 2). One would expect that, after sucrose infusion was discontinued, the sucrose blood level would drop rapidly because of continued diffusion and renal excretion. Once equilibrium had been obtained, the extracellular fluid concentration would slightly exceed that in the blood, since the extracellular fluid would be acting as a reservoir of sucrose for the blood, which in turn is being continually cleared of sucrose by the kidney.

The sucrose disappearance rates of blood and lymph from the normal limb were iden-

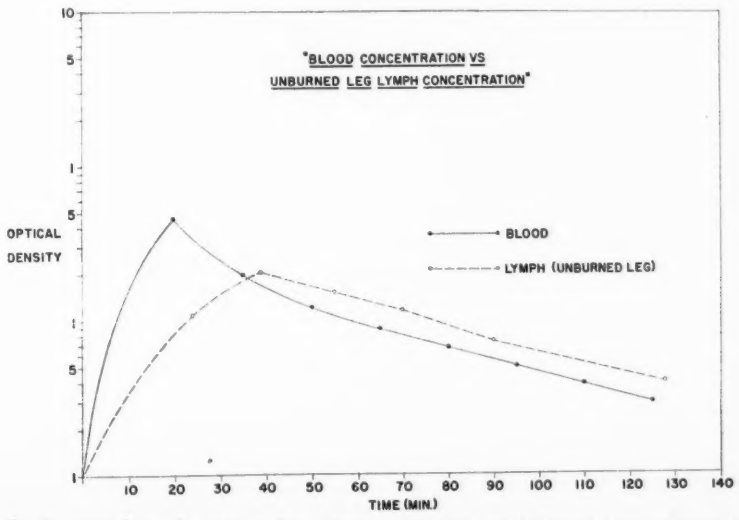

Fig. 2.—A comparison of concentrations of sucrose in blood and in lymph from unburned limb.

tical after apparent equilibrium had been achieved. In all probability, any variation between the disappearance rates would have been masked by the manipulation needed to obtain the later samples of lymph. No assumption or conclusion can be drawn other than to state our findings and the conditions under which they were obtained.

Lymph flow in the thermally injured limb is increased greatly over that in the normal limb. This observation has been reported by Field and co-workers [11] and confirmed by Cope and Moore.[12] Two cubic centimeters of lymph from the burned limb was obtained within two minutes with little or no manipulation or massage. The concentration of sucrose in the lymph from the burned limb increased rapidly and usually reached a peak between 30 and 40 minutes after the infusion was started. Thereafter, the concentration of sucrose began to decrease in a linear fashion when the optical densities were plotted on semilogarithmic paper (Fig. 3).

The finding of sucrose in the lymph of the burned leg almost immediately after the sucrose infusion was initiated establishes the fact that thermal trauma with capillary injury and edema formation does not prevent rapid diffusion of sucrose into the injured area.

The sucrose concentration in the plasma not only is affected by renal excretion but is also directly influenced by the rate and amount of sucrose which is reentering the circulation from the extracellular fluid compartment. The extracellular fluid compartment acts as a functional reservoir of sucrose for the blood stream, as the blood is being continually cleared of sucrose by the kidney. Theoretically, if it were possible to prevent the diffusion of sucrose back into the blood stream from the extracellular fluid, there would be a precipitious fall in blood concentration to zero, as contrasted with the gentle disappearance slopes which are actually found without such a theoretical blockage.

A comparison of the rates of disappearance of sucrose from the blood and from the lymph of the burned limb after apparent equilibrium is found in the accompanying Table. The average disappearance rate for the blood was 0.00696; for the lymph, 0.00307. A paired *t*-test was used to compare the differences in slopes. It was found

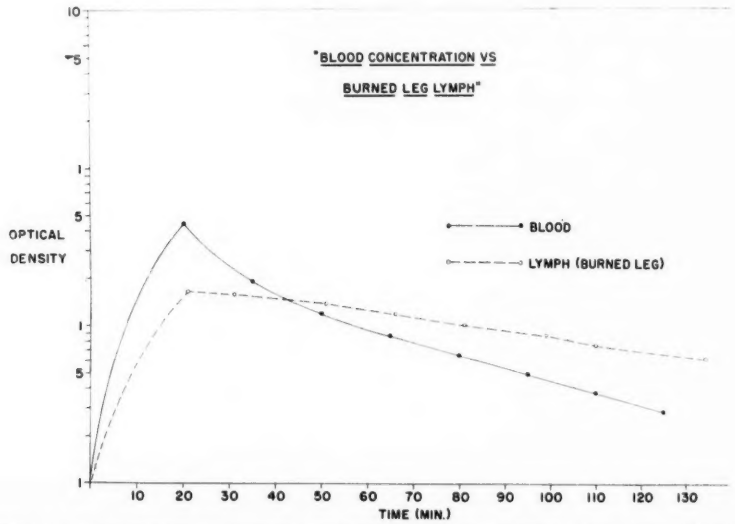

Fig. 3.—A comparison of sucrose disappearance curves of lymph from burned hind limb and of blood.

that there was less than one chance in a thousand of the two slopes being from the same population, $t_{13}=7.20$, while t_{10} for 0.1 significance was 4.59. This substantiates our belief that there is a functional impairment of diffusion of sucrose from the extracellular fluid compartment into the capillary.

After thermal injury the pericapillary area is greatly increased because of edema fluid. Consequently the sucrose in the edematous area cannot diffuse back into the blood stream as rapidly as the blood stream is being cleared of sucrose by the kidney. Owing to the discrepancy in the disappearance rates, it would be expected that the disappearance curve of the blood would eventually lose its apparent linearity. It would, of necessity, have to approach the disappearance rate of the sucrose in the injured area. If this were true, one would be extrapolating a straight line which did not exist.

After thermal injury the disappearance rate of sucrose is more rapid from the blood than it is from the extracellular fluid compartment during the two-hour sampling period. The extrapolation of this faster rate, in turn, gives a plasma concentration at time zero which is unrealistically high. With a larger denominator in the formula $V=\frac{P_o}{I}$, the volume of distribution becomes smaller. Other workers, using S^{35} for extracellular fluid compartment volume determinations in burned humans and dogs, have found reduced extracellular fluid compartment volumes.[13] Since an extrapolation technique was used, their findings were influenced by the same phenomena which were found in this experiment.

The disappearance rate of sucrose from the blood in the normal patient may approximate the actual loss from the extracellular fluid compartment. This is suggested by studies of the blood and normal lymph, which have shown identical rates. However, the manipulation necessary to obtain lymph samples in the normal limb may have

A Comparison of Sucrose Disappearance Rates After Equilibration

Dog	Disappearance Rates		Difference in Rates
	Blood	Lymph of Burned Limb	
1	0.0082	0.0018	−0.0064
2	0.0088	0.0073	−0.0015
3	0.0062	0.0038	−0.0024
4	0.0059	0.0034	−0.0025
5	0.0049	0.0013	−0.0036
6	0.0064	0.0024	−0.0040
7	0.0065	0.0038	−0.0027
8	0.0064	0.0032	−0.0032
9	0.0089	0.0035	−0.0054
10	0.0065	0.0031	−0.0034
11	0.0071	0.0027	−0.0044
12	0.0061	0.0022	−0.0039
13	0.0086	0.0055	−0.0031
14	0.0070	0.0023	−0.0047
Total	0.0975	0.0463	−0.0512
Av.	0.006964	0.003307	−0.003657

Standard Deviation of Difference=0.0019
Standard Deviation of Mean of Difference=0.00051
$t_{13}=7.20$ t_{13} 0.1%=4.59

masked any slight difference between the two disappearing rates.

In 1939, Keeley and co-workers [14] found the plasma volume reduced 38.2% in dogs 5 to 10 hours after thermal injury. This is in keeping with our findings of a reduced extracellular fluid compartment with use of this sucrose technique. Because of the similarity of the reduction in plasma volume and the extracellular fluid volume, it is possible that "functional area" is being measured. If this is true, it would be possible to evaluate various treatments and to determine which treatment restored the functional area to normal size. There are theoretical objections to the hypothesis that we are measuring functional area, because the lymphatic cannulation demonstrated no actual impairment of sucrose diffusion into the edematous areas. It is the decrease in back diffusion from the extracellular fluid compartment which gives a calculated decrease in extracellular fluid volume determinations rather than actual impairment of diffusion into the edematous area.

Summary and Conclusions

In 14 adult mongrel dogs simultaneous blood and lymph samples were taken during and immediately following a sucrose infusion.

The rate of disappearance of sucrose from the blood stream was statistically significantly higher than in the lymph of the burned leg.

Extracellular fluid compartment measurements which use an extrapolation technique are not valid in thermal injury with edema.

The disappearance rates of sucrose in the blood and in the lymph of the unburned hind limb were essentially the same. Manipulation and massage were needed to obtain lymph samples, and no conclusions can be drawn regarding the validity of the sucrose method in the normal animal. Since the disappearance rate of sucrose in the blood is the result of more than one function, in spite of its apparent linearity when plotted on semilogarithmic paper, it is questioned whether extracellular fluid compartment volume measurements using extrapolation techniques are valid in normal subjects.

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Lymphoid Polyps of the Rectum

Report of Three Cases in Siblings

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and
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Lymphoid polyps (benign lymphomata) of the rectum are infrequently reported in the literature. Hayes and Burr collected about 206 cases and added 22 of their own. This condition, which is distinguished from the commoner polyps of the rectum primarily by its microscopic features, was found in 53 of 813 tissue blocks examined by Ehrlich and Hunter, of the Armed Forces Institute of Pathology. All were excised from patients of military age. Helwig and Hansen also reported 70 cases from the Armed Forces Institute of Pathology, all between age 17 and age 62. Li found 2 instances in children, aged 6 and 7, in 49 cases. Barba's case was aged 9. No other cases in childen were found. Harris, reporting 60 cases of polyposis of the rectum in children under the age of 12, noted no instance of lymphoid polyp.

Granet recorded lymphoid polyps in identical twins. This is the only publication we have been able to find which suggests that there may be a familial tendency for lymphoid polyposis. The opportunity to observe this lesion in three siblings under 10 years of age, but not in their parents, stimulated this communication.

Report of Cases

CASE 1.—A 7-year-old Caucasian girl was admitted to Tripler Army Hospital because of rectal bleeding for five days. Questioning revealed that the mother had noted similar streaking of the stools from early infancy. Physical examination revealed no abnormalities outside the lower gastrointestinal tract. Sigmoidoscopy revealed numerous sessile and pedunculated lesions extending from the anus to 7 cm. above the anal verge. The lesions varied from a few millimeters to 2 cm. in diameter at their bases. Biopsies of several lesions were obtained with biopsy forceps. The biopsy specimens were reported as lymphoid polyps of the rectum (Fig. 1). Hemorrhoids and fissures were absent. Barium-enema examination was reported as negative. Treatment consisted of cautery or complete excision of all lesions, approximately 20 in number.

CASE 2.—A 6-year-old brother of the first patient also had a history of blood-streaked stools since birth. Sigmoidoscopic examination revealed several rectal lesions within a few centimeters of the anal verge which were similar in appearance to those of his sister. Biopsy of two or three lesions revealed a similar histologic picture (Fig. 2). There was no evidence of any systemic disease. No further treatment was given.

CASE 3.—A 9-year-old girl, a member of the same family, also had a long history of passing blood-streaked stools. Sigmoidoscopic examination revealed several lesions within a few centimeters of the anal verge similar to those of Case 1 and Case 2. Biopsy of two or three of the lesions revealed a histopathologic picture similar to those of Cases 1 and 2 (Fig. 3). There was no evidence of any systemic disease.

Treatment of Cases 2 and 3 could not be undertaken, as the father was being transferred to another duty station. Follow-up studies have not been available.

The parents of these children underwent sigmoidoscopic examination, but no lesions were found. We were unable to obtain examination of a 6-month-old sibling.

Comment

Lymphoid polyps of the rectum may be discovered at any age, in either sex, and in both Caucasians and in Negroes. The lesions may be single or multiple, are usually sessile, and they vary in size from a few millimeters to a centimeter or more in

Submitted for publication March 9, 1956.

From the Department of Surgery, Tripler Army Hospital, Honolulu, T. H.

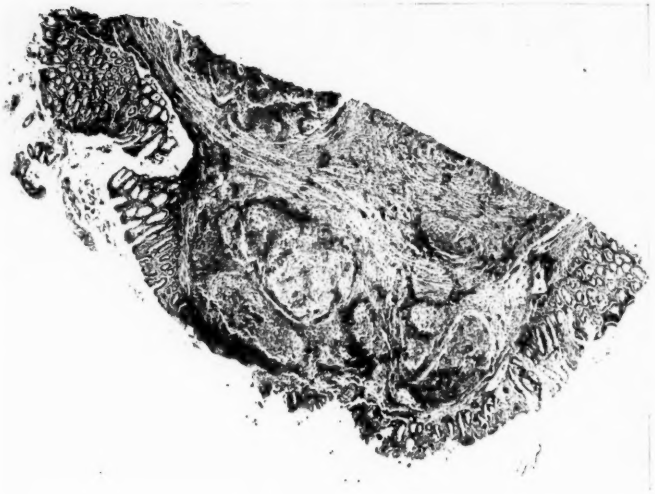

Fig. 1. — Lymphoid polyp of rectum. Large sessile lesion with several small and large lymph follicles in submucosa, most with large germinal centers, elevating mucosa. Focal lymphocytic infiltration of mucosa. Focal atrophy and ulceration of mucosa; reduced ¼ from mag. × 20.

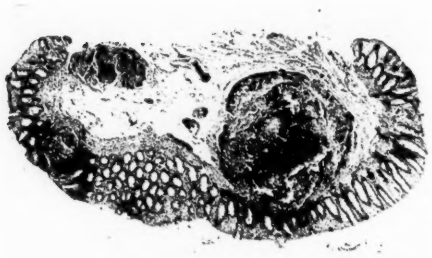

Fig. 2.—Lymphoid polyp of rectum. Sissile lesion with one large and one small lymph follicle in submucosa with rudimentary germinal centers. Lymph follicle with well-developed germinal center in mucosa. Slight focal atrophy of mucosa; reduced approximately 1/6 from mag. × 20.

diameter. They closely resemble and may be grossly indistinguishable from adenomatous polyps of the rectum.

Clinical manifestations include bleeding, mucoid discharge from the rectum, protrusion of a mass from the anus, pain or fullness in the anal region, constipation, or diarrhea. The lesion may be sometimes asymptomatic and discovered in the course of examination of the rectum. Systemic disease of the lymphoid system is not a common accompaniment.

Microscopically the lesion resembles a lymph node in that lymphoid follicles with

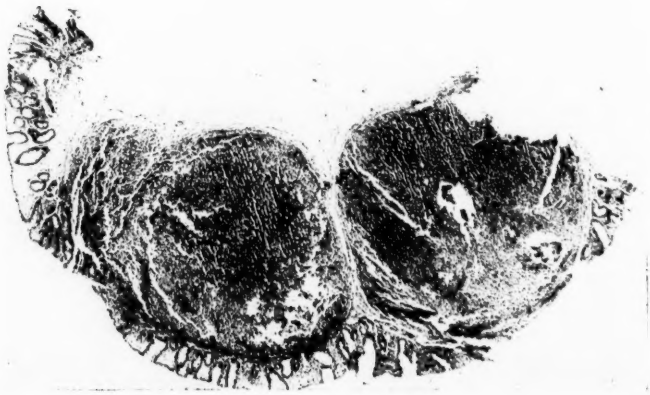

Fig. 3. — Lymphoid polyp of rectum. Sissile lesion with two greatly enlarged lymph follicles in submucosa, one replacing and ulcerating mucosa. Diffuse atrophy and focal infiltration of mucosa with lymphocytes; reduced 1/5 from mag. × 20.

germinal centers are present. However, the characteristic sinusoids of the lymph node are absent. Large histiocytic cells are seen and contain phagocytized cellular debris. The overlying mucosa may be atrophied by pressure, replaced by lymphocytes, or ulcerated. There is no encapsulation of the lesion. There is no extension into the muscularis propria. Microscopic examination is necessary to differentiate benign lymphoid polyps from lymphosarcoma of the rectum. Benign lymphoma is composed of follicles with mitotic figures limited to the germinal center, while lymphosarcomas are composed entirely of small lymphoblasts (lymphosarcoma) or large cells (reticulum-cell lymphosarcoma). Tumors with giant follicles may be difficult to differentiate. If the growth is limited to the mucosa and submucosa the lesion is usually benign. If there is invasion of the muscular coat the growth must be considered a lymphosarcoma. Phagocytosis of cellular debris by the large histiocytic cells is diminished or absent in the malignant lesion.

Most authorities agree that lymphoid polyps of the rectum behave in a benign fashion. However, Barba has suggested that "benign lymphoid hyperplasia of the rectum may resolve spontaneously or have the potential of transformation to a frankly malignant lymphoma." It appears to us important that the diagnosis be clearly established by biopsy of the lesions. Once the diagnosis is established treatment should consist of complete eradication of the lesions by adequate surgical excision, electrofulguration, or a combination of the two. The patient should then be subjected to a long follow-up, with sigmoidoscopic examinations once or twice yearly. The appearance of more lesions would suggest additional biopsy excisions for diagnosis and treatment.

Summary

Lymphoid polyps of the rectum occurring in three siblings but not in their parents are recorded. This may imply a familial tendency which, with the exception of Granet's cases in identical twins, has not previously been noted.

Clinical signs and symptoms of lymphoid polyps of the rectum may include bleeding, mucoid discharge from the rectum, protrusion of a mass from the anus, pain or fullness, constipation, or diarrhea. The lesion may be asymptomatic. Biopsy study is necessary to establish the diagnosis. Current evidence indicates the lesions are benign, and surgical excision or electrofulguration constitutes adequate treatment. Prolonged follow-up of patients with benign lymphoma of the rectum is indicated.

Addendum

A three-year follow-up examination of the three cases was obtained on March 30, 1956, by Col. R. M. Davis, Chief, General Surgical Service, Tokyo Army Hospital, APO 500, San Francisco. His report, in pertinent part, is as follows.

CASE 1.—"She has had no rectal bleeding since that time. Proctoscopic examination was accomplished to a level of 15 centimeters. Examination (was) negative except for a few scattered polypoid projections on the mucosa, each of these about 1 millimeter, and these did not appear to be of clinical significance."

CASE 2.—"Proctoscopic examination was accomplished to a level of 16 centimeters. Examination was negative except for a small punctate scar on the left posterior aspect of the rectum. It was thought that the small scar might be the residual of the biopsy."

CASE 3.—"Proctoscopic examination was accomplished to a level of 22 centimeters. There were a few scattered polypoid projections on the mucosa, each of these measured about 1 millimeter in diameter and appeared to be of no clinical significance."

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Transplantation of the Spinal Cord for the Relief of Paraplegia

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Transplantation is defined as "the grafting of tissues taken from the same body or from another" in the 22d edition of "The American Illustrated Medical Dictionary," by Dorland. Strictly speaking, therefore, the operation herein discussed is not a transplantation, but for many years the moving of a structure to a new location to improve its function has been described as transplantation; for example, transplantation of the ulnar nerve for tardy palsy of the ulnar nerve [1] and transplantation of the spinal cord as described by Hyndman in 1947.[2] Erb and I [3] also felt the term useful and descriptive and we employed it in our paper in 1949.

Transplantation of the spinal cord is most frequently employed in cases of paraplegia due to Pott's disease of the spinal column. Fortunately, owing to improved economic and hygienic levels in the United States and the introduction of agents that are destructive to the organism of tuberculosis, the incidence of tuberculosis has decreased. As a result of the decreased number of cases of tuberculosis the number of cases of Pott's disease with secondary paraplegia also has been decreased. It is likely, therefore, that no one surgeon will see many cases of Pott's disease of the spinal column requiring surgical decompression for paraplegia.

However, knowledge acquired in the handling of one type of disease is often found useful in the handling of other diseases.

As a result of the knowledge gained in decompressing and transplanting the spinal cord for Pott's paraplegia, I have been able to offer help to other unfortunate patients in whom paraplegia has developed because of kyphoscoliosis with encroachment on the domain of the spinal cord.

According to Seddon,[4] Ménard, in 1900, was the first to demonstrate the value of costotransversectomy, a step in many cord transplants, in Pott's paraplegia.

In 1947, Dott [5] reported on the improvement that follows anterior decompression of the spinal cord in the management of Pott's paraplegia. McKenzie and Dewar [6] reported gratifying results in five cases of paraplegia associated with scoliosis. They excluded from their report cases of tuberculosis of the spinal cord producing paraplegia. In their cases of paraplegia secondary to scoliosis they found that compression of the cord was caused by tight dura mater. The compression was relieved by opening the dura on the convex side of the curve. Occasionally rhizotomy, with or without severance of teeth of the dentate ligament, also was performed in order to provide maximal freedom of the cord.

In most cases of Pott's disease of the spinal column with secondary kyphoscoliosis, signs showing involvement of the spinal cord do not develop; in those cases in which the cord is involved the patient may respond to more conservative treatment, rather than a direct attack on the spinal cord. However, it is my opinion that there are cases in which relief of compression or tension on the spinal cord is required if the patient is to be spared a paraplegic life with the many untoward sequelae which are likely to follow the loss of cord function. If, in spite of adequate conservative treatment, the patient's signs of cord involvement fail to

Received for publication Feb. 18, 1956.

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show improvement or the signs increase in severity, then a decision should be made regarding radical operation. It is my feeling that the patient and his family should be told the facts and he should be given an opportunity to accept transplantation of the spinal cord even though at times grave risks are involved.

A decision to move or transplant the spinal cord to a new position necessitates evaluation of the entire picture—that is, the patient's general health must be considered as well as his heart function, pulmonary reserve, and renal function. It is also necessary to determine whether or not there is activity in a tuberculous lesion of the spinal column and whether or not tuberculous lesions are present in other organs.

Again, transplanting the spinal cord in cases of Pott's paraplegia does not, of course, minimize the necessity of treatment of the tuberculous or other lesions that might be present. Whole-hearted cooperation with the specialist in the field of tuberculosis is needed. Judicious use of antibiotic and other drugs which have been shown to be extremely important in the treatment of tuberculosis is mandatory. For the best possible results transplantation of the spinal cord for paraplegia should be handled on a combined service with internist, orthopedist, neurologist, physiatrist,* and neurosurgeon working as a team.

In transplanting the spinal cord all pressure from products of inflammation (pus and granulation tissue) and bony and cartilaginous tissue, as well as all tension on the deficient cord, should be removed (Figs. 1-4). In order to do this it is often necessary to divide one or more nerve roots extradurally. Since this operation is usually performed for lesions involving the thoracic portion of the spinal cord, there is no seri-

Fig. 1.—Anteroposterior view of the spinal column of a 28-year-old man with paraplegia secondary to Pott's disease of the spinal column with marked kyphosis.

Fig. 2.—Lateral view of the spinal column of same patient illustrated in Figure 1.

* The professional physiatrist, the physician who has been well trained in physical therapy and rehabilitation, is, in my estimation, one of the most important members of the team. It is he who can make the efforts of the internist, neurologist, orthopedist, and neurosurgeon blossom forth in a rehabilitated person who can care for himself and be gainfully employed. Without his help the rest of the work might be in vain. Particular mention should be made of Dr. Earl Elkins, head of the department of physical medicine and rehabilitation at St. Marys Hospital, for his untiring efforts in behalf of these unfortunate paraplegic patients.

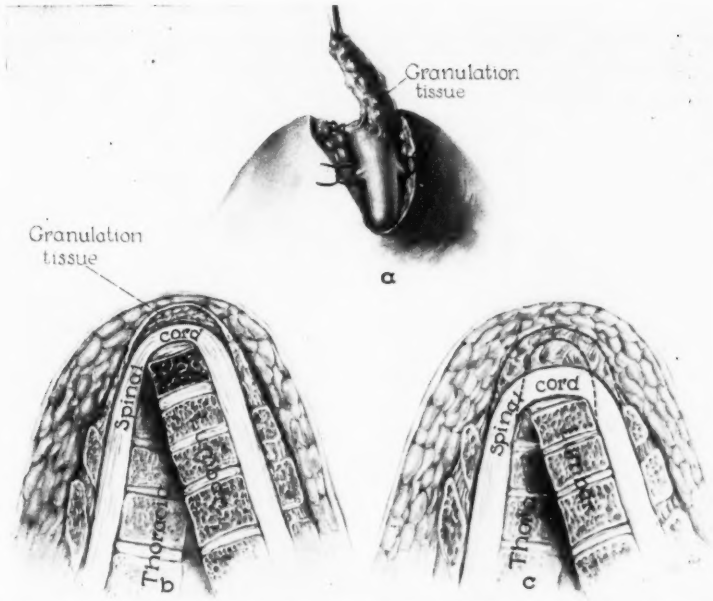

Fig. 3.—Artist's drawings made at time of transplantation of the spinal cord in case illustrated in Figures 1 and 2, showing the marked angulation and compression of the spinal cord at apex of the kyphos by tuberculous bone and granulation tissue. In drawing (*c*) the relief of cord compression is shown after the removal of the diseased vertebral body and the extradural granulation tissue. The spinal cord has been transplanted anteriorly.

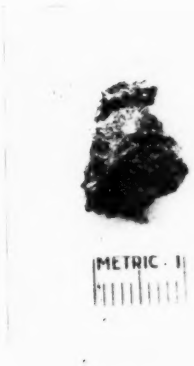

Fig. 4.—Intraspinal granulation tissue removed at time of transplantation in case illustrated in Figures 1 to 3.

ous impairment after the rhizotomy. A neurosurgeon would hesitate to divide a lumbar or sacral root; likewise he would not want to divide one of the roots from the fifth cervical to the first thoracic root, inclusive, because these roots innervate the extremities, and it is the function of the extremities that he is trying to preserve or restore.

The spinal cord may be transplanted in one of three directions—anteriorly in cases of true kyphosis, laterally (to the concave side) in scoliosis, and anterolaterally in cases of kyphoscoliosis.

It is important in operating on the spinal column to maintain stability. In order to do this as little of the supporting bone as is absolutely essential should be removed—it must, however, be enough to relieve pressure and tension on the spinal cord.

In cases of Pott's paraplegia it is usually possible to do a costotransversectomy, remove the products of inflammation (pus and granulation tissue), divide one or more

nerve roots, and remove vertebral body tissue and intervertebral disk tissue that are compressing the cord in front and transplant the cord to a new position free of pressure and tension while preserving the laminae, the spinous processes, and the articulating facets and pedicles on the opposite side. In some cases it is advisable to perform a bone-graft fusion of the spinal column at the same time. On occasion, it is preferable to delay the fusion until a later date in order to minimize the danger of postoperative clot with further compression of the cord. In several of the patients on whom I have operated the spinal column has been fused with a bone-graft transplant previously. In such cases it is important to preserve the graft and operate beneath and lateral to it.

Occasionally the bone graft, although appearing well healed in the roentgenograms, may be involved with tuberculous osteomyelitis. In such a case the involved portion of the graft must be removed to get rid of the pus and granulation tissue which may be contributing to the spinal cord symptoms.

Eleven cases in which the spinal cord was transplanted form the basis for this report. In 6 of the 11 cases the spinal cord was transplanted because of paraplegia secondary to Pott's disease of the spinal column. There was no question of the lesion being due to tuberculosis, and in the majority of cases the tissue (pus or granulation tissue) supplied at the time of operation to the bacteriologist was found to be positive both on guinea-pig innoculation and on culture. Brief reviews of the other five cases in which the spinal cord was transplanted follow.

In one case, that of a man 65 years of age at the time the spinal cord was transplanted, the lesion was thought to be tuberculous, but bacteriologic methods did not prove the presence of tuberculosis. The patient stated that he had sustained a spinal injury at the age of 4 years (61 years prior to operation) and that paralysis of his legs had developed. He reported that at the age of 4 years a hay rack in which he was riding went over a bump and his back was injured. He became paralyzed from his waist down and could not control his bowels or bladder. He was bedridden for two years and then walked with the aid of crutches for two additional years. At this time excessive curvature of the upper portion of his back was noted. Six months before registering at the Mayo Clinic he noted that he was dragging his right foot. This disability continued to increase in severity up to the time of transplantation of the spinal cord.

Another man, 53 years of age, had his spinal cord transplanted because of paraplegia due to kyphoscoliosis which was thought most likely due to tuberculosis, although the presence of this disease could not be proved by bacteriologic methods. He had had a deformity of the lower thoracic portion of his spinal column since the age of 6 years and had had progressive signs of cord compression for three years before he submitted to operation, although I had advised him on three different occasions over a period of a year to have an operation before his spinal cord was irreparably damaged.

A 17-year-old boy[3] had his spinal cord transplanted because of paraplegia due to kyphoscoliosis secondary to a congenital fifth thoracic hemivertebra (Figs. 5 and 6).

A young man 22 years of age had his spinal cord transplanted because of paraplegia due to kyphoscoliosis secondary to von Recklinghausen's neurofibromatosis without intraspinal neoplasm.

The 11th patient to undergo transplantation of the spinal cord was a child 13 years of age who had paraplegia due to kyphoscoliosis of the paralytic type. The history suggested a birth injury with superimposition of anterior poliomyelitis at the age of 1½ or 2 years.[3]

Although the basic etiologic factor was not the same in each case, the primary indication for transplantation of the spinal cord was paraplegia of varying degrees due to kyphosis or kyphoscoliosis. The idea

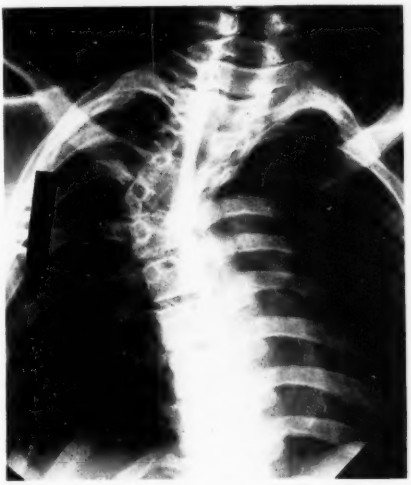

Fig. 5.—Preoperative anteroposterior view of the spinal column of the 17-year-old boy who had paraplegia secondary to kyphoscoliosis due to a fifth thoracic hemivertebra. The well-healed bone graft placed elsewhere is clearly shown. The fifth rib on the left is absent.

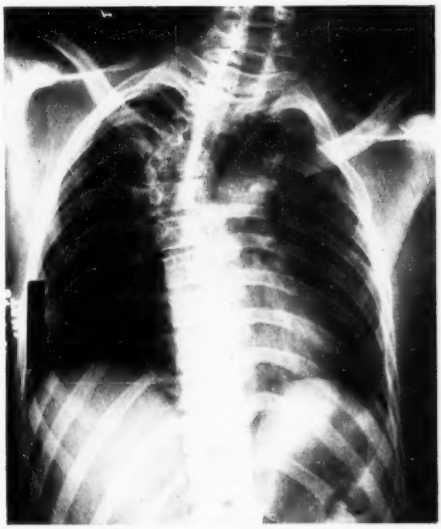

Fig. 6.—Postoperative anteroposterior view of spinal column of case illustrated in Figure 5. The left costotransversectomy of thoracic vertebrae 3, 4, and 6 can be seen and also the silver clips on the divided nerve roots. The bone graft was not disturbed.

was to free the involved portion of the spinal cord of pressure or tension or both. To do this it was necessary to remove tissues about the cord and move the cord to a different position.

Should a Diagnostic Lumbar Puncture Be Performed Before Transplanting the Spinal Cord?

If there is any doubt about the diagnosis and there seems to be a probability that a neoplasm may be present, then the spinal fluid should be checked for hydrodynamics and total protein. I agree with Hyndman that a spinal puncture should not be done in the presence of tuberculosis of the spinal column, for fear of introducing the organism of tuberculosis into the subarachnoid space.

In only 4 of the 11 cases here recorded was spinal puncture done.

A puncture was done on the 22-year-old patient known to have von Recklinghausen's disease. There was no block, and the total protein was 60 mg. per 100 cc. of fluid.

The 65-year-old man who had had kyphosis for 61 years and motor weakness for only 6 months underwent spinal puncture. Spinal block was not indicated on Queckenstedt's test, and the total protein was 100 mg. per 100 cc. of fluid.

Puncture was performed on the 17-year-old boy with kyphoscoliosis due to a hemivertebra and complete paraplegia suspected elsewhere as being due to a tumor on the spinal cord. There was complete subarachnoid block, with a total protein of 300 mg. per 100 cc. of fluid.

The 13-year-old boy with paraplegia due to kyphoscoliosis considered secondary to a birth injury and paralytic poliomyelitis underwent puncture of the cisterna magna and iophendylate (Pantopaque) myelography to locate the site of compression of the spinal cord. An attempt to obtain spinal fluid in the lumbar and thoracic regions of the spinal column had been unsuccessful. Three cubic centimeters of iophendylate revealed a complete subarachnoid block at the fourth thoracic vertebra. The total protein in the fluid removed from the cisterna magna measured only 10 mg. per 100 cc.

Results of Transplantation of the Spinal Cord for Paraplegia

In three of six cases of paraplegia due to Pott's disease of the spinal column the results of transplantation of the spinal cord were excellent. These three patients were able to return to gainful occupations and to get around without handicap.

The results of the other three patients having Pott's disease of the spinal column were not so encouraging. One patient, when last heard from, had experienced little or no change from his preoperative status. He had had cord signs for one year prior to operation. Another patient's paraplegia was aggravated, and when last heard from she was still confined to bed. A man experienced marked improvement after transplantation of the spinal cord for Pott's kyphosis and was able to run his farm. Later, however, due to reactivation of his tuberculous lesion and a fall, paraplegia recurred. He is to have another operation on his spinal column soon.

Results in the remaining five cases of the group are as follows.

The 65-year-old man whose kyphosis with secondary paraplegia was thought to be due to Pott's disease did not show any change.

The 53-year-old man whose lesion was thought, but could not be proved, to be tuberculous and who had signs of compression of the cord for three years was immedietely worse, and then he improved.

The 17-year-old boy who had kyphoscoliosis and complete paraplegia secondary to a fifth thoracic hemivertebra has made a complete recovery and is now studying to be a dentist, seven years after his operation.

The 22-year-old man whose paraplegia was based on kyphoscoliosis secondary to von Recklinghausen's disease showed marked improvement and is able to walk without aid, whereas before the spinal cord transplant he could get about only with the aid of two crutches.

The other patient, the 13-year-old boy who had a paralytic kyphoscoliosis with paraplegia, has shown marked improvement. Prior to operation his neurologic examination revealed a sensory level for all modalities at the fourth thoracic dermatome; he was unable to move either lower extremity voluntarily, but mass reflexes were bothersome.

The condition looked hopeless as far as any return of function to the cord was concerned, but, due to the patient's youth and the understanding and cooperative parents, who were anxious of course to improve the boy's condition, we agreed to operate on the patient.

A neurologic recheck 14 days after operation did not reveal essential change in the patient's condition. Four months later, when the patient returned for a check-up, general motor and sensory improvement was noted. Four years later due to continued improvement he was able to get around with only one cane. He was able to go fishing, to ride a bicycle, and to attend school regularly.

All of the cord transplants in this series were for kyphosis or kyphoscoliosis in the thoracic region of the spinal column. There were no postoperative deaths, and there have been no deaths since the patients were last seen or heard from.

The youngest patient was 13 years of age at the time of operation and the oldest, 68 years of age. The average age was 38.5 years. There were nine males and two females in the series.

Conclusions

A review of a series of 11 cases in which transplantation of the spinal cord was carried out for paraplegia due to a variety of etiologic factors resulting in kyphosis or kyphoscoliosis establishes the operation of transplantation of the spinal cord as a useful procedure in a small number of carefully selected patients.

The spinal cord should be transplanted before irreparable damage to the cord has occurred. If the patient's neurologic signs fail to show improvement on adequate conservative treatment or the signs progress while the patient is under observation and

treatment, a decision should be made regarding the risks of not operating and the definite risks which attend surgical procedures for such lesions.

The patients whose paraplegia has been present for a relatively short time show better recuperative powers than those who have been paralyzed for years. Likewise, as in many other morbid conditions, youth seems to be in the patient's favor. The youngest patients in this series had the most remarkable results; two patients who were thought to be hopelessly paralyzed have made a complete and an excellent recovery, respectively.

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Carcinoma of the Ampulla of Vater

Case Report of Nine-Year Survival of an Elderly Woman

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Since 1935, when Whipple, Parsons, and Mullins [1] reported a radical two-stage pancreaticoduodenectomy for carcinoma of the ampulla of Vater, considerable attention has been focused on this procedure as a possible means of treatment for both ampullary and pancreatic tumors. The number of long-term survivals has been small, however, and, as Kaufman and Wilson [2] point out, through 1955 only 21 cases of five-year survival following resections of ampullary carcinoma have been reported in the American literature. Part of the reason for this is the relative rarity of the lesion. In the years between 1920 and 1936, Lieber, Stewart, and Lund [3] could report only 14 cases in 22,152 autopsies at the Philadelphia General Hospital. At the Cincinnati General Hospital between 1937 and 1946, Siler and Zinninger [4] reported only 8 cases among 31,935 patients admitted to the surgical service.

Not all long-term survivals have followed radical resections, however. Koerte * performed a local resection which was followed by 22 years' survival. Dennis and Varco [6] also report a patient living and well 12 years 8 months after a local resection. However, in the same communication they cite a second case of local resection where there were no apparent metastases in which recurrence required radical excision four years later. Although at the time of the second procedure there were no gross evidences of metastases, the patient died seven years later, apparently of abdominal carcinomatosis.

In 1899, William Halsted [5] reported the first successful attempt to remove a carcinoma of the ampulla by resecting a duodenal segment and the pancreas adjacent to the ampulla and anastomosing the pancreatic and common ducts to the duodenum. The patient died six months later from recurrent carcinoma. It was not until Siler and Zinninger's report, in 1948,[4] that the first five-year survival following radical pancreaticoduodenal resection was recorded in this country. As the number recorded since then is still small, it seems justifiable to report a nine-year survival following a radical two-stage resection of ampullary carcinoma.

Report of Case

The patient first entered Colorado General Hospital on Nov. 16, 1946, at the age of 72. She had been well until one year previous to admission, when her stools began intermittently to become clay-colored and her urine dark. During the three months before admission, she had recurrent chills and fever. One month before admission, her physician noted that she was jaundiced, and a bile test of her urine was strongly positive. One week before admission she went into shock and was admitted to her local hospital; on the following day she passed a tarry stool and was then transferred to Colorado General Hospital. She had no knowledge of weight loss during the previous year.

Physical examination revealed a somewhat emaciated, markedly jaundiced woman, with a temperature of 103.6 F; pulse, 104; blood pressure, 110/65; respirations, 20. Positive findings in addition to her jaundice were as follows: liver enlarged 4 finger-breadths below the costal margin and slightly tender, gall bladder palpably enlarged. Laboratory findings were as follows: hemoglobin, 9.3; white blood cell count, 7600; cephalin flocculation, 3+; van den Bergh, 7.5 direct; urine, 1+ bile. A gastrointestinal series

Received for publication May 20, 1956.

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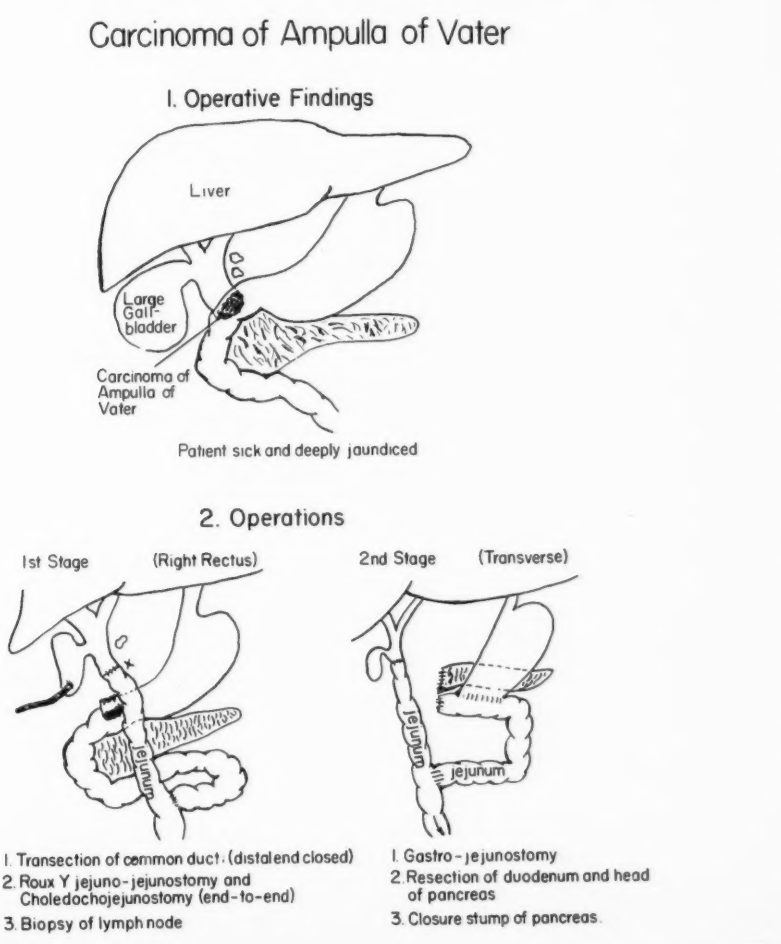
* Cited by Parsons.[11]

showed abnormally rapid filling of the pylorus and duodenum. A chest x-ray was negative. Duodenal washings were negative for malignant cells.

It was thought that her jaundice was due to bilary obstruction, and after vitamin K therapy and transfusions, she underwent exploratory laparotomy through a right rectus incision on Dec. 5, 1946. The liver and gall bladder were found to be markedly enlarged. For spatial facilitation the contents of the latter were aspirated. The common duct was then located and found to be enlarged to 3.5 cm. in diameter. Within the duodenum a firm mass 2×3×4 cm. in size could be felt. This was thought to be an ampullary carcinoma. Since there was no evidence of metastasis, a first-stage pancreaticoduodenectomy was performed. A Roux-Y jejunostomy was done, using 12 in. (30.5 cm.) for the proximal limb. The common duct was transected 1 in. above the upper duodenal margin, and the distal end was closed by the Parker-Kerr technique. The proximal portion of the common duct was then sutured end-to-end with the distal limb of the jejunum, the two being approximately equal in size. The gall bladder was opened more widely, and multiple stones were removed. A 16 F. catheter was sewed to the opening and brought out through a separate stab wound, and the gall bladder was sewed to the peritoneum. The abdomen was then closed. The patient tolerated the two-and-a-half-hour procedure well.

One month later (Jan. 2, 1947) the second stage was done through a transverse incision. After orientation had been completed, the stomach was divided above the pylorus, and the distal end was closed. The proximal end was anastomosed to the



jejunum 3 in. (7.6 cm.) distal to its emergence behind the ligament of Treitz. The duodenum was divided at its third portion and the distal end closed. Dissection was carried proximally, keeping a margin of the pancreas attached. A small nick was inadvertently made in the duodenum, exposing the ampullary carcinoma, but no spillage of tumor occurred. The main pancreatic duct was ligated and the open end of the pancreas sewn shut with continuous absorbable surgical suture. After closure of the wound, the patient was returned to the ward in good condition. The operative time was four hours.

Pathologic diagnosis was adenocarcinoma of the ampulla of Vater. No metastatic disease was found, either grossly or microscopically.

Her postoperative course was marked by gradual recovery and gain in weight. She required 10 grains (0.6 gm.) of pancreatin q. d., starting nine days postoperatively. Since her discharge, on Feb. 2, 1947, one month after operation, she has been seen regularly every six months and was last seen on May 15, 1956.

Comment

The fact that the patient was elderly (age 72), debilitated, and had had symptoms for some time led the medical service to believe that she had little hope for recovery. The fact that she has fully recovered demonstrates the point that old age and debility do not necessarily preclude the possibility of cure. Even as a palliative operation, Orr [7] has pointed out that pancreaticoduodenectomy deserves consideration. Child and his associates [8] compared the results of palliative bypassing operations to pancreaticoduodenectomy. In a review of over 1000 cases treated by the first method, the average length of life was 7.5 months; in 13 cases treated by pancreaticoduodenectomy, the average survival time was 15 months.

Numerous methods of performing radical pancreaticoduodenectomy are reported. Modifications of the two-stage procedure were proposed by many, including Whipple,[12] Orr,[13] Hunt,[14] Cooper,[15] and Illingsworth.[16] Whipple,[17] although at first an advocate of a two-stage method, later preferred a one-stage procedure, as did Child.[18] Among Whipple's reasons were the avoidance of two operative procedures and anesthesias and the avoidance of the difficulties of extensive vascular adhesions at the second procedure. In the case herein reported, the second stage was considerably more difficult by virtue of massive adhesions. The two-stage procedure in this instance, however, was elected because it was felt that the patient was too ill to withstand anything but a primary diverting operation.

It is also of interest that the pancreas was sewn shut and no pancreatic duct anastomosis made in this case. It has been reported that in order to reduce or prevent the complications of poor fat and protein absorption with concomitant diarrhea, pancreatic anastomosis is desirable.† Whipple [10] and his associates, however, have stated that ligation of the main pancreatic duct does not lead to serious complications. At least in this case the patient has not had difficulty with either malnutrition or diarrhea. She gained weight rapidly postoperatively and has maintained her weight well. She is still taking pancreatin.

Summary

A case report of a nine-year survival of adenocarcinoma of the ampulla of Vater treated by pancreaticoduodenectomy in an elderly debilitated patient is presented.

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Anesthetic Properties of Trifluoroethyl Vinyl Ether and Common Ethers

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The purpose of this investigation is to compare the anesthetic effectiveness of one of the less explosive ethers, trifluoroethyl vinyl ether, with well known ethers.

It is known that halogenation of organic compounds decreases their flammability. The substitution of chlorine atoms in the methane molecule shows progressively decreasing flammability to where the triple and tertiary substituted compounds, chloroform and carbon tetrachloride, can be used as fire extinguishers. Halogenation also increases toxicity, e. g., carbon tetrachloride is an anesthetic but lethal at surgical levels. Fluorine has the same property of diminishing flammability in compounds but is less toxic and more stable. Trifluorethyl vinyl ether (Fluoromar) is a colorless liquid having a pleasant, sweetish odor. The physical properties of the ethers used in these studies are given in Table 1.

In studies of trifluorethyl vinyl ether by Krantz and co-workers, in 1953,[1] four dogs and one monkey were anesthetized by means of an anesthesia machine. The quantities of diethyl and trifluoroethyl vinyl ether required to produce comparable anesthesia were thought to be about equal. Induction time for trifluoroethyl vinyl ether was equal to that of diethyl ether and greater than that of ethyl vinyl ether. All three ethers were considered equal in potency with regard to quantities of ether required for induction and respiratory arrest.

Orth and Dornette, in 1955,[3] report that in open-drop anesthesia in children the

Submitted for publication April 7, 1956.

The trifluoroethyl vinyl ether (Fluoromar) used in these experiments was supplied by the Ohio Chemical & Surgical Equipment Company.

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TABLE 1.—*Physical Properties of the Ethers*

Property	Trifluoroethyl Vinyl Ether CF_3CH_2 / $CH_2=CH$ \ O	Ethyl Vinyl Ether C_2H_5 / $CH_2=CH$ \ O	Divinyl Ether $CH_2=CH$ / $CH_2=CH$ \ O	Diethyl Ether C_2H_5 / C_2H_5 \ O
Boiling point, degrees C	42.7	35.8	28.4	34.6
Vapor pressure, mm. of Hg at 20 C 40 C	 295 670	 428 ---	 553 1145	 442 921
Specific gravity of liquid 20 C	.13	0.76	0.77	0.71
Gas density (air=1)	4.4	2.5	2.4	2.6
Lower Flammability limit in O_2 Air	 4.0% 4.2%	 2.2% ----	 1.9% 1.7%	 2.0% 1.9%
Minimum spark ignition energy, millijoules for 3% of vapor in dry O_2 4% 6% 8%	 ---- ---- 0.30 0.08	 high 0.13 0.02 0.01		 0.30 0.05 0.01 0.01
Solubility in water, ml./100 ml.	0.4	0.8	0.7	8.0

loss of consciousness with trifluoroethyl vinyl ether is as rapid as with ethyl chloride. It exceeds that of divinyl and ethyl vinyl ether. Surgical anesthesia was accomplished in one to two minutes for infants and children and in two to four minutes for adults.

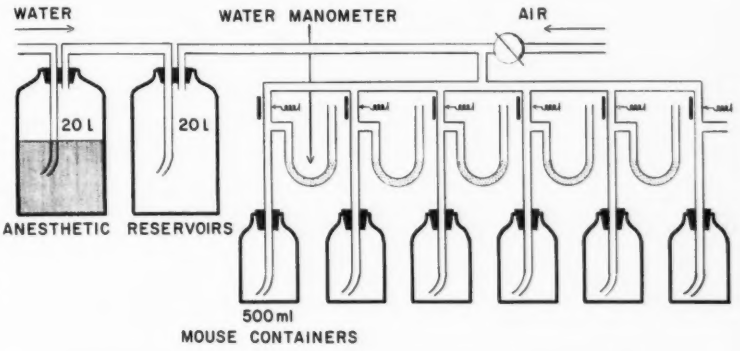

Fig. 1.—Diagram of the experimental apparatus. The inlet tubes extend to the bottom of the mouse containers to insure thorough mixing and flushing of the anesthetic vapors. One manometer is not shown.

They also found recovery of consciousness in one to two minutes, which equals or exceeds the time of recovery after nitrous oxide or cyclopropane.

Method and Procedure

Mice were used in these experiments because their small size and high metabolic rate make possible a complete cycle of anesthesia and recovery within a short period of time. In 81 experiments, 486 male and female mice weighing 20 to 32 gm. were used. They had free access to food and water at all times and were not reused for seven days. At least three experiments with six mice in each were performed for any given concentration.

The ether vapor was mixed with air in two 20 liter bottles and distributed through a flow-equalizing manifold to six separate 500 ml. milk bottles each containing a mouse (Fig. 1). The flow to each mouse bottle was regulated by a screw clamp and read on a water manometer. Waste gases were exhausted through a hole in the mouse bottle stopper.

Before each experiment the system was flushed with compressed air to remove vapors left over from previous experiments. The weighed mice were placed in the containers which were ventilated by compressed air. At zero time the compressed air was stopped, and the cages were flushed in five seconds with 3 liters of the ether-vapor mixture. The flow was thereafter maintained at 2 liters per minute. After 10 minutes of exposure to the anesthetic, compressed air was flushed through the system for the recovery period.

Since 1 gm. molecular weight of vapor occupies 22.4 liters under standard conditions, any given concentration can be calculated from

$$\text{Grams of ether} = \text{vol.\% ether} \times \frac{\text{MW} \times \text{reservoir volume}}{22{,}400}$$

Corrections for preservatives in the ethers and for atmospheric pressure and temperature were made with the following equation:

$$\text{Milliliters ether at room P and T} = \frac{273 \times 760}{T_{lab} \times (P_{lab} - \text{v.p. } H_2O) \times \text{purity} \times \text{density}}$$

The depth of anesthesia was estimated each minute and was expressed numerically according to a modification of the Guedel classification as shown in Table 2. During induction the mice exhibited clear signs as listed in the table, with very little overlapping of stages. The signs were not as clear during recovery.

Results

The experimental data were expressed as graphs drawn from the average depth of anesthesia for all experiments at a given concentration. The curves show great regularity for the induction, but some variability occurs in the recovery period (Figs. 2, 3, 4, and 5.).

To compare the ethers, Fig. 6 has been drawn from the data at 10 minutes. The

TABLE 2.—*The Guedel Classification of Anesthetic Stages as Modified for Mice*

Stage of Anesthesia	Numerical Factor	Signs of Anesthesia in Mice
Normal	1	Unaffected by anesthetic agent; may show signs of irritation
I	2	Staggering, wobbling, loss of coordination
II	3	Marked twitching; regular or irregular respiration
III 1 & 2	4	Little or no movement; regular respiration
III 3 & 4	5	Respiratory difficulty; paradoxical respiration
IV	6	Respiratory arrest

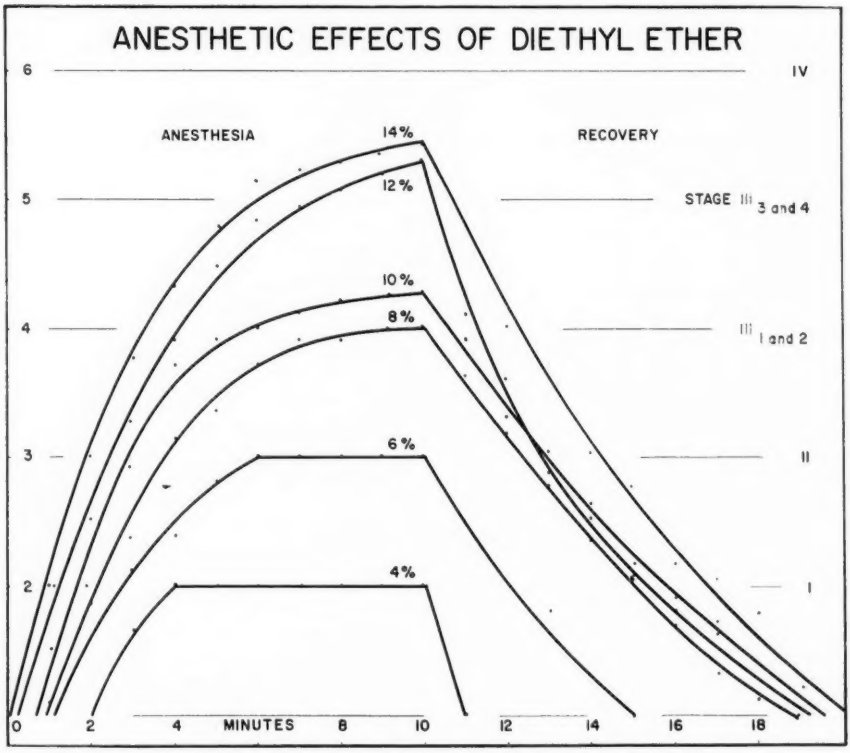

Fig. 2.—The anesthetic effects of diethyl ether.

concentration of ether has been plotted against the depth of anesthesia. Margin of safety is represented by the slope of the curve and is least for the greatest slope.

Diethyl ether is seen to produce anesthesia beginning at 9 vol.% and respiratory arrest at 15 vol.%. It has a margin of safety of 6 vol.%, the largest of any of the ethers studied. If potency is defined as the level of concentration required to produce anesthesia, then diethyl ether is the least potent of the series.

Ethyl vinyl ether is represented by a line nearly parallel to the line for diethyl ether

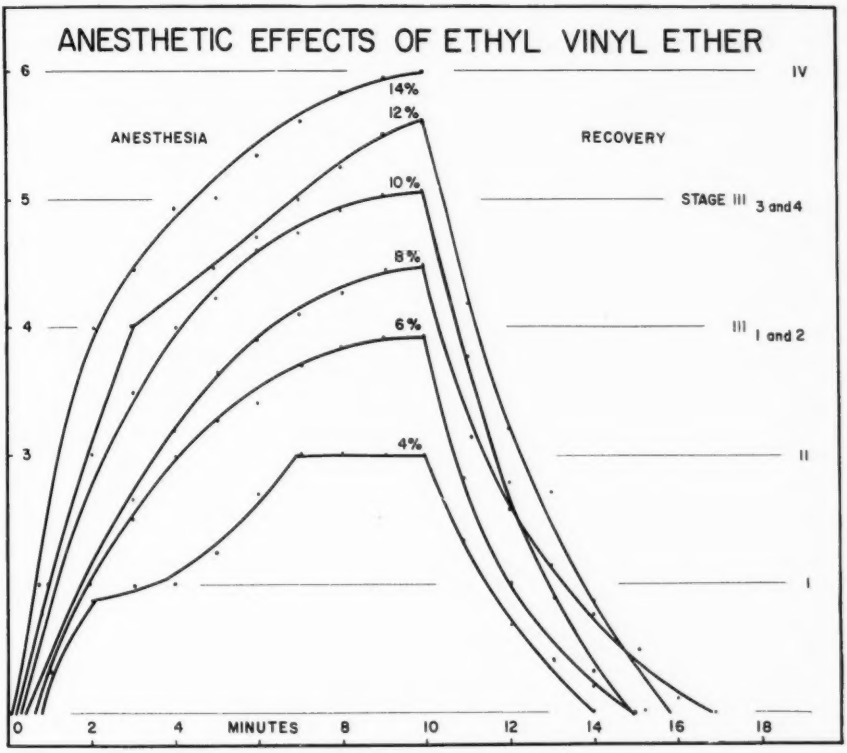

Fig. 3.—The anesthetic effects of ethyl vinyl ether.

but above it at all points. Anesthesia occurs at a concentration of 7 vol.% and respiratory arrest at 13 vol.%, with a 6 vol.% margin of safety. It can therefore be considered more potent than diethyl ether but with an equal margin of safety. Its recovery period as shown in Fig. 3 is shorter than that of diethyl and longer than that of divinyl ether.

Divinyl ether requires 8 vol.% concentration to produce anesthesia and only 12 vol.% to cause respiratory arrest, giving it a margin of safety of 4 vol.%.

Trifluoroethyl vinyl ether has a curve identical to that of divinyl ether, which indicates equal potency and margin of safety. Trifluoroethyl vinyl ether has the advantage of being the only ether in the series with a pleasant smell and little irritative effect.

A test of significance made on the curves of Fig. 6, by Mr. K. A. Brownlee, of the Committee on Statistics at the University of Chicago, shows the statistical reliability of our conclusions. An analysis of variants was made on the data by partitioning the concentration effect into linear, quadratic, and remaining components. The interaction of concentration with the type of ether was similarly partitioned. The results show that divinyl ether and trifluoroethyl vinyl ether are correctly stated as a single line ($P > 0.5$ for separate lines). The slopes of diethyl and ethyl vinyl ether are similar with a probability of 90% to 95%. A significant difference between the slopes formed by divinyl and trifluoroethyl vinyl ether and the slope common to diethyl and ethyl vinyl ether has a probability of 99.5%. The study also showed the validity of expressing the curves of Fig. 6 as straight lines.

The results of these present experiments are similar to those previously done by

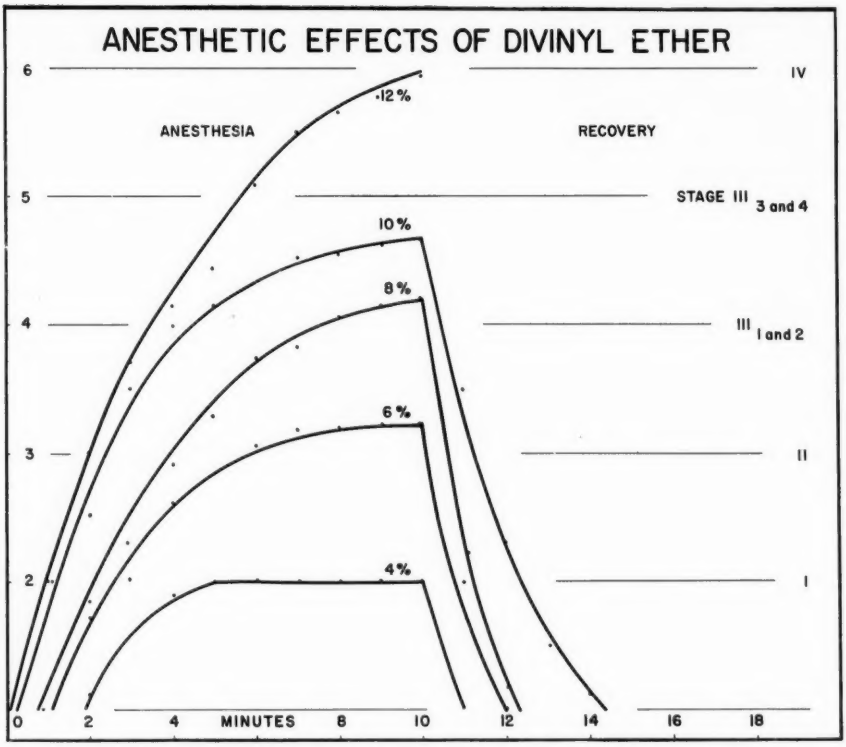

Fig. 4.—The anesthetic effects of divinyl ether.

Morch, Aycrigg, and Berger.[2] Using only three of the present series of ethers, they too found that ethyl vinyl ether has effects intermediate to those of diethyl and divinyl ether. The curves of the present set of experiments show faster onset of anesthetic effect and greater response to a given concentration, probably on the basis of more efficient apparatus.

The onset of anesthesia occurred in these experiments with nearly the same rapidity for all four ethers investigated (Figs. 2, 3, 4, and 5.). Diethyl ether produced surgical anesthesia nearly as fast as did the same concentration of divinyl ether. Because of the irritative effects of diethyl ether on the respiratory tract, it is not possible under clinical conditions to induce a patient as rapidly as with divinyl ether.

Limited clinical trial by open-drop method seems to show that induction occurs less rapidly with trifluoroethyl vinyl ether than with divinyl ether. The difference in rate of induction is probably caused by the difference in rate of evaporation, because the boiling point of trifluoroethyl vinyl ether is 44 C, while divinyl ether boils at 28 C. The lower speed of evaporation of trifluoroethyl vinyl ether offers a factor of safety because this almost nonirritating anesthetic could otherwise produce too deep anesthesia in a very short time. Trifluoroethyl vinyl ether by open-drop administration gives slower induction than divinyl ether, but recovery time for both is equally rapid.

Summary

An improved method to compare the anesthestic properties of ethers is presented.

Diethyl and divinyl ethers are used as reference drugs.

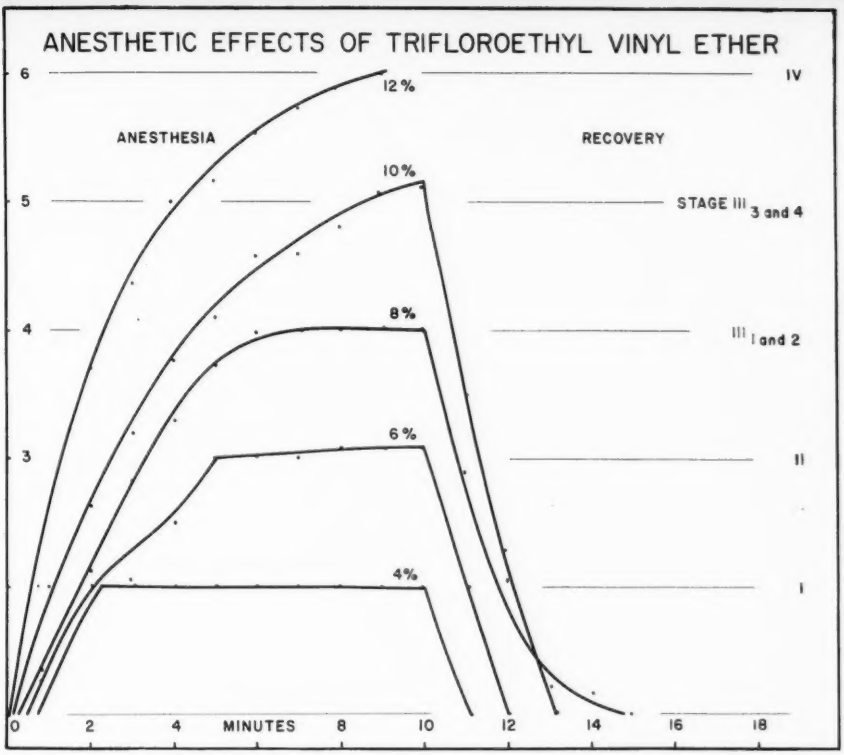

Fig. 5.—The anesthetic effects of trifluoroethyl vinyl ether.

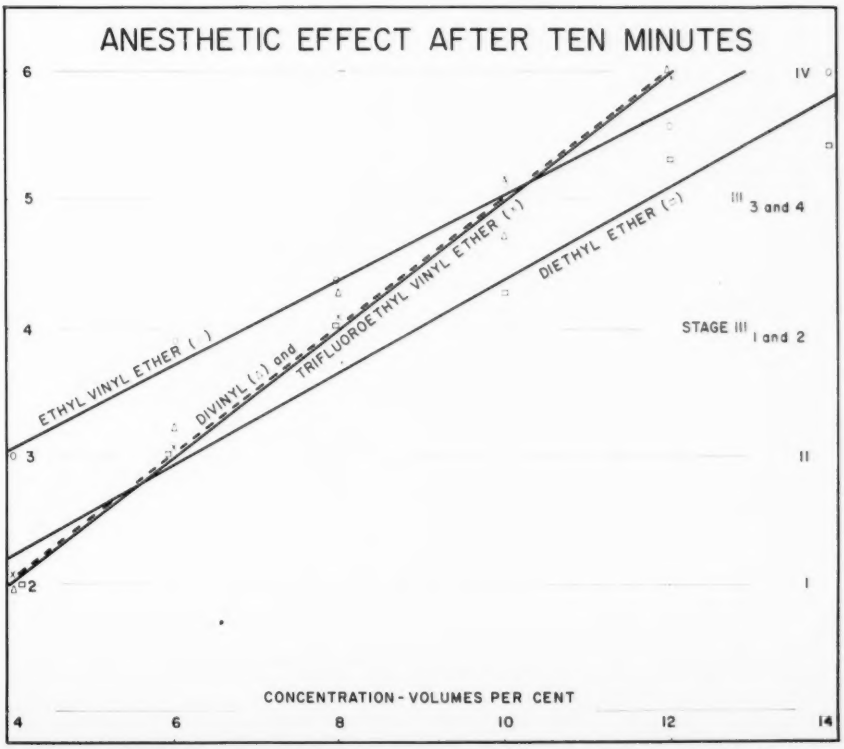

Fig. 6.—Anesthetic effect after 10 minutes. The data for divinyl and trifluoroethyl vinyl ether fall along the same line.

Ethyl vinyl ether is found to have anesthetic properties intermediate to those of diethyl and divinyl ether. It is more potent than diethyl ether at all concentrations, but it has the same margin of safety. Ethyl vinyl ether is more potent at surgical concentrations than divinyl ether but has a greater margin of safety.

Trifluoroethyl vinyl ether is found to have anesthetic properties equal to those of divinyl ether with regard to potency and margin of safety.

Trifluoroethyl vinyl ether is practically nonirritating and has a pleasant smell.

In clinical anesthesia using open-drop administration, the induction is slower with trifluoroethyl vinyl than with divinyl ether, but the recovery time is the same.

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Diverticulosis of the Gall Bladder

Rokitansky-Aschoff Sinuses and Calculi Demonstrated Roentgenographically

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More than a century ago, Rokitansky* mentioned hernia-like outpouchings of the gall-bladder mucosa. He described them as sometimes numerous and usually very small, commonly having narrow openings, and at times containing small concretions. Halpert,[3] in 1927, declared these formations identical with the structures described by Aschoff in 1905 as Luschka's ducts and named them Rokitansky-Aschoff sinuses.

These diverticula may extend to the muscular layer of the gall-bladder wall, may penetrate into the intermuscular lacunae, or may progress through the muscular wall into the underlying connective tissue, even reaching the serosa occasionally. Although structurally similar to diverticula of the small intestine, colon, and urinary bladder, they differ in their tendency toward folding and branching, a characteristic ascribed to the particular construction of the gall-bladder wall. Pathologicoanatomic study has demonstrated that these invaginations are more numerous, appreciably deeper, and more developed in chronically inflamed gall bladders than in normal gall bladders and that they increase in number with increasing age.[4]

The Rokitansky-Aschoff sinuses may contain bile, bile pigment, cholesterol crystals, and, at times, typical biliary concretions. Inflammatory changes may be present or lacking altogether. Presumably, increased pressure in the gall bladder is a causative factor in the initial changes. Inadequate functional adaptation of the organ, due to lack of muscles in its mucosa and lack of submucosa, apparently brings about weakening of the contractile elements present, while chronic overdistention widens the intermuscular septa. Thus, the lack of musculature in the mucosa and the loose arrangement of the muscular bundles, most likely to occur in association with chronic inflammation, permit the herniations to take place.

Roentgenographic Aspects

Although Rokitansky-Aschoff sinuses are commonly observed in pathologic specimens, particularly those exhibiting signs of chronic cholecystitis, they have been demonstrated roentgenographically infrequently and only relatively recently. Visualization of this phenomenon was first reported in 1948 by March.[5] In 1955, Ross, Finby, and Evans[6] summarized 11 collected cases, adding 2 of their own,† and 2 other cases were reported.‡ In only 4 of these 15 cases was cholelithiasis demonstrable. The 16th case, presented here, is the 5th in which stones were visualized. Of the 16 patients, 11 were women, and the ages ranged from 22 to 57 years, averaging 45. In well over half of the cases, there was a narrowed luminal segment, but in less than a third was there evidence of calculi.

In all these cases symptoms suggestive of cholecystitis prompted the roentgen examination. Pain in the right upper quadrant of the abdomen and intolerance to fatty foods were the chief complaints. Usually, there

Submitted for publication Jan. 26, 1956.

From the Department of Radiology, St. Luke's Hospital.

* References 1 and 2.

† In an addendum, Ross, Finby, and Evans[6] stated that since their paper was submitted for publication they had seen five additional cases of intramural diverticulosis of the gall bladder demonstrated on cholecystography, but they gave no details.

‡ References 7 and 8.

was a history of attacks occurring intermittently over a prolonged period.

The roentgen appearance of this anomaly is unique, presenting no appreciable problem in differential diagnosis once it is identified. The diverticula extending to the muscular layer are not demonstrated by present roentgenographic methods, according to Ross, Finby, and Evans.[6] Those penetrating into the intermuscular lacunae, however, appear as fine linear shadows of contrast material adjacent to and paralleling the contrast material in the lumen of the gall bladder. The protrusions through the muscular wall extending into the underlying connective tissue and occasionally reaching the serosa present the characteristic roentgenographic picture. Around the lumen of the gall bladder, an irregular group of somewhat rounded densities forms an interrupted concentric ring. This "corona" or halo-like extravasation of the contrast material beyond the normal lumen of the gall bladder is typical of intramural diverticulosis, portraying as it does "a composite picture of numerous, contrast-filled, closely packed, plentifully branched and cryptically dilated diverticula." [9]

The infrequency of roentgenographic demonstration of diverticulosis of the gall-bladder wall is understandable when one considers the nature of the diverticula and the conditions favorable to visualization of these mucosal invaginations. According to Åkerlund and Rudhe,[9] the requisites are a gall bladder well filled with contrast material of adequate density and diverticula sufficiently large, numerous, closely packed, and branched, with patent communicating channels and orifices, and also free of appreciable amounts of retained bile components, such as mucus, detritus, or concretions, which interfere with contrast filling. Small stones within the diverticula, when opaque, appear to lie outside and to be unrelated to the visualized organ. In addition, an inflammatory process with edema and occlusion of the lumina of the channels communicating with the gall bladder will hinder or prevent recognition of the diverticula.[10] Obviously, ideal conditions for visualization doubtless are fulfilled only in exceptional cases. Perhaps newer contrast materials for use in cholecystography will make possible increasingly frequent roentgen diagnosis of this condition.

The consensus is that roentgenographic visualization of Rokitansky-Aschoff sinuses is an indication for cholecystectomy, since these intramural diverticula are associated with inflammatory disease and cholelithiasis.[6] In over half of the cases reported, there was roentgen evidence of a constriction in the proximal portion of the gall-bladder lumen. Increased pressure within the gall bladder, attributed to this narrowed segment, is believed secondarily to cause enlargement of the intramural protrusions into demonstrable diverticula. Even when this constriction is not demonstrated, there may be partial obstruction resulting from inflammatory change, thick secretions, or small calculi obstructing the cystic duct. In making these observations, Ross, Finby, and Evans [6] expressed the opinion that in view of the probable relationship of the intramural diverticula to inflammation and increased pressure within the gall bladder, their penetration through the muscular wall into the underlying connective tissue is probably accompanied by exacerbations of symptoms and the possible complications of acute inflammation, cholelithiasis, and perforation. They noted also that a thickened gall-bladder wall, present in about half of the cases they reviewed, is not always associated with diverticula penetrating through the muscular wall into the underlying connective tissue and probably is a manifestation of the inflammatory process.

Report of a Case

A 45-year-old white woman was admitted to St. Luke's Hospital on Feb. 11, 1954, as an outpatient, referred by her family physician for cholecystography. For three weeks she had had typical attacks of gall-bladder colic, with severe pain in the right upper quadrant of the abdomen, radiating to the chest, shoulders, and both arms,

accompanied by nausea and vomiting. The pain was relieved by subcutaneous injection of meperidine (Demerol) hydrochloride.

The patient was a well-developed woman presenting no evidence of gross abnormality on physical examination. Urinalysis and examination of the blood gave normal results.

A cholecystogram following administration of 3 gm. of iopanoic acid (Telepaque) demonstrated a gall bladder of fairly average size, constricted at the neck, showing an excellent concentration of the contrast material and the presence of numerous small nonopaque shadows representing cholesterol calculi. In addition, a concentric interrupted rim of opacification surrounding the lumen of the gall bladder represented contrast-filled Rokitansky-Aschoff sinuses (Fig. 1). After the fatty meal, the gall bladder showed no contraction, but the linear shadow bordering the gall bladder was much more clearly defined (Fig. 2).

Cholecystectomy was advised, but deferred.

The attacks recurred less frequently thereafter until Aug. 8, 1954, when the patient was admitted to St. Vincent's Hospital for cholecystectomy. At that time, the chief complaint was pain in the right hypochondrium, and the preoperative diagnosis was cholecystitis with cholelithiasis. Six months had now elapsed since cholecystography had demonstrated the presence of the intramural diverticula and cholelithiasis. At no time in this interval was there evidence of jaundice or change in color of the stool or urine.

Physical examination was noncontributory, except for slight tenderness in the right upper quadrant of the abdomen. The results of urinalysis were negative, except for a trace of albumin, and the specific gravity was 1.022. Examination of the blood showed the hemoglobin estimation to be 12.5 per 100 cc. (82%), the red blood cells numbered 3,990,000 and the white blood cells 8350 per cu. mm. The differential count was 58% neutrophiles, with 53% segmented forms and 5% band forms, 37% lymphocytes, 2% monocytes, and 3% eosinophiles.

Cholecystectomy was performed by Dr. Edward Canipelli on Aug. 9. The gall bladder was thickened, but no acute inflammation was present. One large stone and a number of small stones were palpable within the gall bladder, and a number of tiny black faceted stones, measuring 1 to 2 mm. in diameter, were present in the cystic and common ducts. The common duct was greatly re-

Fig. 1.—Cholecystogram vaguely demonstrating the interrupted concentric ring of contrast material surrounding the gall bladder and also showing constriction at the neck of the gall bladder. In addition, numerous small calculi are visible.

Fig. 2.—Following the fatty meal, the halo-like rim of contrast material filling the Rokitansky-Aschoff sinuses in the wall of the gall bladder is much more clearly demonstrated, although no contraction of the gall bladder is evident.

duced in caliber, especially at the junction with the cystic duct. A polyethylene catheter was inserted in the cystic duct and the duct tied to it. The gall bladder then was excised and the catheter removed. A rubber T-tube was placed in the common duct. Because of the small caliber of the duct, it was almost severed, but was closed without difficulty around the tube.

On pathologic examination, the gall bladder measured 8 cm. by 3 cm., and the wall measured up to 0.7 cm. in thickness. The mucosa was rough, and numerous black faceted stones of varying size were present in the lumen. Stones were impacted in the cystic duct. Microscopically, sections through the gall bladder showed many of the villi intact and the mucosa bile-stained. Numerous intramural diverticula extended well into the subserosa (Fig. 3), and there was a moderate chronic inflammatory reaction (Fig. 3). The serosa was edematous. The pathologic diagnosis was chronic cholecystitis and intramural diverticulosis with cholelithiasis.

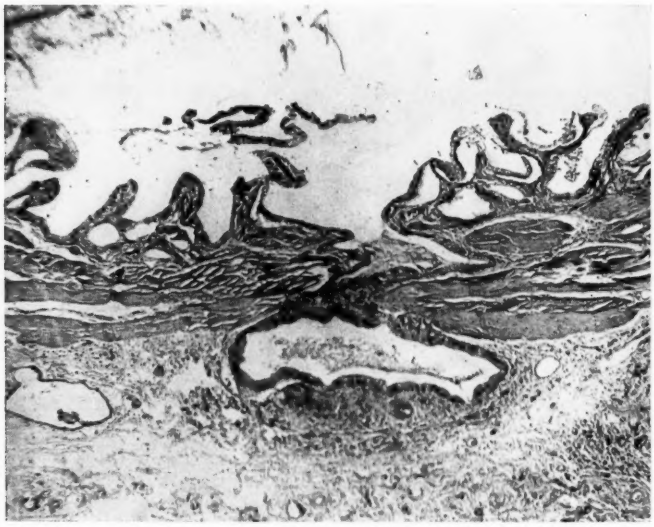

Fig. 3. — Photomicrograph of a postinflammatory intramural diverticulum extending from the gall-bladder lumen into the subserosa. Hematoxylin and eosin; reduced about 1/9 from mag. × 120.

The postoperative course was without incident, and the patient was discharged from the hospital on Aug. 23, 1954. Since the operation nearly two years ago, the patient has experienced no attacks of pain in the upper portion of the abdomen and has remained in good health.

Comment

The present case of diverticulosis of the gall bladder conforms clinically, roentgenographically, and pathologically to the general pattern of the 15 cases previously described in the literature.[1] The roentgenographic appearance of the gall bladder with its unique border was characteristic of Rokitansky-Aschoff sinuses. As in other reported cases, the excellent concentration of the contrast material suggested no great degree of functional impairment of the gall bladder from chronic cholecystitis. The halo-like rim of contrast material framing the gall-bladder shadow was typical and was more clearly defined after the fatty meal, although the gall bladder did not contract. In a number of the cases reported, following the fatty meal there was contraction of the gall bladder, as well as clearer definition of the surrounding border.

In this fifth case to be reported in which cholelithiasis was demonstrable roentgenographically, not only were calculi present in the lumen of the gall bladder but also in the cystic and common ducts. While there was no narrowed segment of the body of the gall bladder in this case such as was present in a number of the other cases, there was constriction at the neck, and there was also pronounced constriction of the common duct, particularly at the junction with the cystic duct, in which stones were impacted.

As Ross, Finby, and Evans [6] pointed out, partial obstruction from such reduced caliber and impaction may be a source of increased pressure within the gall bladder, which, in turn, promotes enlargement of the Rokitansky-Aschoff sinuses to demonstrable size.

The thickened wall of the gall bladder in this case, as in others, was indicative of the chronic cholecystitis. The presence of numerous intramural diverticula penetrating into the subserosa was likewise characteristically associated with the inflammatory process.

Summary

Roentgenographic demonstration of an interrupted beaded rim of contrast material, characterized by irregularly distributed more or less rounded opacities, appearing immediately adjacent to and following for varying distances the anatomic contour of the visualized gall bladder, is indicative of diverticulosis of the gall bladder.

A case is reported in which Rokitansky-Aschoff sinuses were demonstrated roentgenographically. There was also roentgen evidence of calculi in the lumen of the gall bladder. These roentgenographic findings were confirmed on pathologic examination. This case apparently is the 16th to be reported in which these intramural diverticula were demonstrated and the 5th in which calculi were visible on roentgen examination.

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Open Surgical Drainage for Hepatic Amebic Abscess

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Of all the complications of amebiasis, amebic liver abscess is the commonest and most serious as regards mortality and morbidity. For many years the consensus has been that amebic abscess of the liver should be treated medically because of the unusually high mortality associated with this condition. Kean,[1] in 1953, reported on six patients at Halloran General Hospital with amebic liver abscess treated with emetine and chloroquine diphosphate without recourse to surgery. Spellberg,[2] as recently as 1954, said "Surgical drainage is inadvisable because of its higher mortality and morbidity owing to secondary infection." He advised that only those cases with demonstrable secondary infection, with multiple abscesses, and with solitary left-lobed abscesses be considered as suitable candidates for open surgical drainage.

After a thorough review and study of the problem, Jordon[3] suggested that these original ideas regarding open surgical drainage be revised. His paper reviews the most recent work on the problem; the use of the sulfanilamides, the use of the antibiotics of the tetracyline series, and open surgical drainage, alone and in combination. He compares his own mortality and morbidity figures with those in the previous reports. He has definitely shown a marked reduction in both mortality and morbidity percentages by this combined method. This report and our own results in a small series of cases indicate that this combined treatment is the method of choice in this very serious condition.

Submitted for publication April 5, 1956.

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Etiology, Pathogenesis, and Material

Invasion of the liver by Endamoeba histolytica is secondary to the primary disease in the intestine, as outlined by Rodgers,[4] in 1922. There is always some more or less mild liver damage with the onset of the intestinal phase, but actual abscess formation may not occur until many years after the initial intestinal infection has occurred, been treated, or forgotten. This is very important.

In Honduras, intestinal amebiasis is very common,[5] complicated in a large percentage of patients by an amebic hepatitis, yet the incidence of an actual amebic liver abscess is small. Factors such as the numbers and virulence of the parasite, individual host resistance and the presence or absence of secondary infection are universal factors that determine subsequent abscess formation. Locally, such factors as deficient nutritional states, chronic alcoholic hepatitis, nonspecific hepatic dysfunctions, associated parasitic infections and intoxications, and generally disturbed biochemical and/or physiological processes are a few of the other factors to be considered here. Their actual role is yet to be determined.

The local incidence of intestinal amebiasis[6] is much higher than that in the United States, so naturally the incidence of amebic liver abscess must be correspondingly higher. Spellberg[2] says that 5% of patients with intestinal amebiasis may develop hepatic complications and liver abscess. Yet the actual number of cases of liver abscess

seen do not approach the estimate. During the last two years we have personally observed and treated 275 surgical patients at the Casa de Salud El Carmen in Tegucigalpa, Honduras. (1) Twenty-five per cent of these patients had an active asymptomatic amebic infection at the time of observation that had been present for one year or more. (2) Eighty per cent of these same patients gave a clinical history of amebiasis at some time during their lifetime. (3) Thirty per cent of these same patients had signs and symptoms of a previous amebic hepatitis which was not recognized at the time of the original infection. In Honduras amebic hepatitis does not present clinical or biochemical evidence of jaundice. In spite of these high incidence rates for intestinal amebiasis, only six patients had proved amebic liver abscess. This is an incidence of 8.7%, 2.7%, and 8.3% for each of the three groups mentioned.

Clinical Manifestations and Diagnosis

Hepatic amebic abscess may present a varied clinical picture. The youngest patient in our series was 12 years of age, and the oldest patient was 55 years of age. Three patients were men, and three were women. The abscess in all of the patients was limited to the right lobe of the liver. In no patient was there extension of the abscess or perforation of the same into the peritoneal cavity. In two patients there was extension of the abscess into the right thoracic cavity, one by direct continuity and one by hematogenous spread.

The time interval between the onset of the intestinal disease and its hepatic complication is unknown. Manson-Bahr [7] states that hepatic abscess formation rarely occurs under 6 months and may take up to 57 years to develop. Our patients had symptoms of liver pathology for one month in two cases, two months in one case, and four months in three cases. Jordan's [3] five cases apparently fall into the rare group, since the clinical picture was rather acute in all, being under one month's duration.

All of the patients in this series complained of pain in the right upper quadrant, most marked over the liver area. The pain was described as dull and aching. There was tenderness on palpation along the mid and anterior axillary lines. Upward enlargement of the liver was manifested by an elevation of the diaphragm. Downward enlargement was noted by palpation of the liver edge up to 4 fingerbreadths below the costal margin. In two cases the liver mass extended almost to the umbilicus and well onto the splenic area on the left.

Fever and chills were present in four cases. The fever was of the intermittent type, spiking towards nightfall and not returning to normal. In all of the patients the fever had preceded the liver pain and liver enlargement. Fatigue, loss of weight, loss of energy, and anorexia were noted in five patients. All had to discontinue their usual work because of these complaints. These symptoms, likewise, had preceded the specific liver manifestations by several weeks. These six early manifestations are nonspecific. The patients believed that they were suffering from (1) malaria, (2) intestinal amebiasis or typhoid fever, and (3) influenza.

Manifestations of a gastritis with dyspepsia were present in three patients. Meat and/or meat products were poorly tolerated. Belching, gaseous distention, hunger pains, and flatulence were common. None of the patients had hematemesis or melena.

Three of the patients had a productive cough accompanied in two by chest pains. These pains were pleuritic in character, aggravated by deep respiration. Reflex splinting of the right lower chest was observed in all of these three patients. Expectoration was present in two of these three patients and was a thick tenacious, reddish black, foul-smelling material. Tuberculosis was suspected in two of these patients.

None of the patients had diarrhea on admission to the hospital. All of the patients had been treated prior to the present illness

Data on Treatment of Patients

Case No.	Date Clinically Proved Amebiasis	Treatment of Original Infection		Dates Subsequent Attacks Amebiasis	Treatment of Second Infection		Date Diagnosis of Abscess	Hospitalized Stool, Sputum		Pus
		Courses	Duration		Courses	Duration		On Admission	After Treatment	
1	1948	1	10*	No record	0	0	1952	Neg. 12† Pos.	Neg. 7*	....
2	1950	1	21*	1951 1952	2	30* 7*	1952	Pos.	Neg. 7*	....
3	1950	0	0	No record	0	0	1952	Pos.	Neg. 14*	Pos.
4	1938	1	180‡	1942 1944 1950	3	0 0 10	1953	Pos.	Neg. 28*	Pos.
5	1910	0	0	No record	0	0	1953	Pos.	Neg. 10*	Pos.
6	1950	3	30‡ 45‡ 20‡		3	14‡ 0 7	1953	Neg. 2† Pos.	Pos. 7* Neg.	Pos.

* Days of treatment under medical supervision.
† Days after hospitalization.
‡ Days of treatment, sporadic and without medical supervision.

for amebiasis on one or more occasions at varying intervals of up to 10 years or more (Table). Five of the patients recalled a diarrhea of moderate degree within one year of the present illness, and all recalled having had diarrhea within two years of the present illness. Three of the patients had positive stool examinations on the day of admission to the hospital, and five of the patients had positive stool examinations on repeated occasions within three days of hospitalization. The stools showed the presence of both trophozoite and cyst forms of E. histolytica. In two of the patients with the productive cough, the parasite was identified on both saline and iodine smears about seven days after hospitalization. Our failure to find the parasite after six specimens had been examined corroborated the statement of Anderson [8] that "six negative specimens ruled out the diagnosis of amebic infection."

Roentgenograms revealed elevation of the right diaphragm with limitation of its mobility. Five of the patients presented a cresentic doming of the diaphragm, which we have considered as pathognomonic of the disease. In American medical literature, attention has been called to an eccentric elevation of the diaphragm above the abscess. This observation has not been noted locally in the patients seen by us. There was blunting of the costophrenic angle in all of the radiograms studied. In one case there was evidence of cavitation in the lower lobe of the right lung.

None of the complement-fixation tests or their various modifications were performed.* Laboratory findings were a moderate leucocytosis, an eosinophilia, increased urinary biliary pigments, positive stool for E. histolytica with increase in the coliform bacteria, and liver-function tests within normal ranges.

Needle aspiration should be done once the diagnosis of liver abscess has been made. This is not a difficult procedure and does not increase the morbidity or mortality. All of the patients in this series had "chocolate sauce" or "anchovy paste" pus that is typical of amebic abscess of the liver. Active ameba were identified in the material aspirated from five of the patients. There were no pyogenic bacteria present on direct smears, and cultures were not done.

* References 9 and 10.

Management and Operative Technique

Amebic liver abscess is usually confined totally to the parenchyma of the liver but may, via direct extension, perforate into any of the six subphrenic spaces, the pleural cavity, and the peritoneum. None of our cases showed peritoneal extension, and two had pleural involvement. The treatment and operative technique is the same in all cases.

Initial treatment is directed towards eradication of the parasite from the intestinal tract, the liver, and the abscess itself. This treatment must be intense, prolonged, and combined with adequate supportive measures to ensure success. The patient is considered as ready for surgery when cured of his intestinal phase. This is determined when there have been three consecutive negative stools at 48-hour intervals. If the patient shows signs of progressive hepatic involvement, increasing toxicity, etc., it is unwise to wait for the three negative stools before open surgical drainage is performed. The supportive measures are instituted to combat dehydration, avitaminosis, toxemia, malnutrition, and associated parasitic infections.

The patients are hospitalized and under constant supervision. The routine is as follows.

(1) Absolute bed rest, without exercise and effort, is essential.

(2) Restoration of the biochemical, physiological, and vitamin imbalances by the best methods adapted to each individual patient.

(3) Intense antiamebic medication as soon as the diagnosis of amebiasis is made. The drugs most successful in our hands have been 5,7- dicloro-8-oxyquinaldine, an emetine preparation, and an antibiotic of the tetracycline series. The dosage of the drug will vary with the individual response of

the patient, but is usually massive to ensure a rapid disappearance of the parasite from the intestinal tract.

(4) Open surgical drainage of the abscess. This can usually be done in 12 days.

Surgical exposure of the liver is difficult, and the choice of approach depends upon the location of the lesion—in this instance the right lobe. The induction of anesthesia is with thiopental (Pentothal); the patient is intubated and anesthesia continued with ethylene-ether. Blood and dextrose solution are administered during the operation, and curare is used for more complete relaxation.

The initial incision is a modified Singleton incision close along the right costal margin, extending outward from the xiphoid process to just beyond the nipple line. The anterior sheath of the rectus muscle and the external oblique muscle are divided. The rectus muscle is retracted medially, the posterior sheath of the rectus muscle is then divided, and the internal oblique muscle, transversalis muscle, and peritoneum divided in the line of the fibers of the internal oblique muscle. The abdomen is explored, the extent and size of the abscess is determined, and its point of fluctuation is localized. Once these points have been fixed, the original incision is extended downward via a right transrectus incision to just above the umbilicus. Hemostasis must be complete before further manipulation is done.

Adhesions about the liver, if any, are preserved to avoid spillage of infected material into the peritoneal cavity or any of the surgical spaces about the liver. If there are no adhesions, the peritoneum is carefully protected with gauze packs well impregnated with a solution of erythromycin 1:1000. The intestines are packed off first with saline packs, then the stomach is pushed to the left, and further exposure is obtained as for a partial hepatectomy. The moist packs impregnated with the antibiotic solution are not allowed to become dry.

The operative field is now completely exposed. The point of least resistance of the abscess is determined again. Through this point a trocar is inserted and connected to a suction machine. The abscess cavity is now evacuated under intermittent suction. Once no more purulent material is obtained, the abscess cavity is flushed three or four times with an isotonic saline solution warmed to body temperature, followed by another irrigation with an emetine hydrochloride solution. Bleeding from the cavity wall is not usually marked because of the thick capsule surrounding the abscess cavity.

Once drained, a small area of the abscess surface is removed about the size of a silver dollar. Two or three 20 F. or 22 F. Pezzer catheters are placed within the cavity and are held in place with long nonabsorbable (cotton) surgical sutures placed through the catheters and liver parenchyma to reach the outside with the ends of the catheters. Powdered gelatin sponge, absorbable (Gelfoam, The Upjohn Company), is instilled into the cavity, and the edges of the cavity are approximated with deep through-and-through sutures running well into normal liver parenchyma. These sutures are tied without tension over long strips of gelatin sponge. Complete approximation cannot be expected.

Penrose drains are placed in the foramen of Winslow, beneath the gall bladder bed, the anterior superior subphrenic space, and behind the first part of the duodenum, if indicated. These are brought out through the original skin incisions, the Pezzer catheters are exteriorized through a lateral stab wound without twisting or tension, and the abdomen is closed in layers in the usual manner.

Postoperative care consists of a continuation of the intense antiamebic therapy instituted preoperatively, intravenous fluids and vitamins for the first 24 hours, and early ambulation. During the first 24 hours almost continuous irrigation of the abscess is maintained, using a combination of erythromycin and emetine hydrochloride. During this time the drainage is copious and foul, but within 36 hours it begins to diminish in amounts and usually ceases totally about the fourth to fifth day. The most dependent cavity drain is allowed to remain in until

the last and is removed on about the seventh day. During this time the Penrose drains have been shortened daily after the first 48 hours. The patient is usually ready for discharge from the hospital in about two weeks under this management. We have had no deaths, no wound disruptions, and no secondary wound infections.

Comment

Open surgical drainage for amebic liver abscess has been done only when the abscess was secondarily infected, had developed other complications, or had involved the left lobe of the liver. It was not until 1947 [11] that this procedure was considered a safe and feasible undertaking.

Since the advent of the antibiotics, their use in amebic abscess of the liver has been reported by various authors.† They showed that the use of the antibiotics did not replace adequate drainage. The French [16] believe that open surgical drainage is no longer associated with a higher mortality or morbidity than the usual conservative measures.

In this small series of six patients with amebic abscess of the liver, all, including two with pulmonary involvement, were treated by a combined medicosurgical technique. Under this routine the patient was ready for surgery in from 7 days (the shortest period of time) to 27 days. The average time required for preoperative preparation was 12 days. Postoperatively, the patients could be discharged from the hospital in from two to three weeks. Prior to this time, hospitalization was from 6 to 12 weeks. In all the patients the signs and symptoms of infection dramatically subsided on opening and draining the abscess. The patients returned to the outpatient department for another two to three weeks for dressings and to ensure complete closure of the wound. All patients were closely checked from six months to one year after surgery for relapse or recurrence. None was found. The period of morbidity was reduced 30% in all of the patients.

† References 13-15.

The diagnosis of an amebic hepatitis early in its course, with adequate prolonged treatment, will eliminate the chance of abscess formation. In this regard Smitskamp's [17] work on the effect of emetine on human sedimentation rate will serve as an effective method of differentiation. In amebic hepatitis the sedimentation rate is reduced, whereas in amebic liver abscess the sedimentation rate remains elevated or unchanged. This test was not performed in any of the patients of this report. Except in those cases with acute yellow atrophy of the liver (very rare) or where there is clinical evidence of extensive functional liver damage, a therapeutic trial with emetine or one of its derivatives will not harm the patient.

Certain variations in the disease seen in Honduras can be mentioned. Of the six patients reported, three were men and three were women. All the abscesses were in the right lobe of the liver and were solitary abscesses. Signs and symptoms of active intestinal amebiasis were present in all of the patients within one year of the present illness. Active amebas were found in the abscess pus in four of the six patients subjected to surgery. In the United States the reports indicate that more men are affected by the disease than women. Similarly, 85% of the abscesses occurred in the right lobe and 15% in the left lobe of the liver. Seventy per cent of the abscesses were solitary, and thirty per cent were multiple. Spellberg [2] observed active intestinal amebiasis in only 60% of his patients with amebic liver abscess. The parasite is reported as found only with difficulty in the abscess pus. The eccentric elevation of the diaphragm reported by Milles, Capps, and Ettinger [18] as characteristic was not seen in any of our patients.

Conclusions

Amebic abscess of the liver is usually secondary to an attack of intestinal amebiasis which has provoked an amebic hepatitis in the patient. The original intestinal infec-

tion may or may not immediately precede the liver involvement. Inadequately treated intestinal amebiasis, or lack of treatment, lowered host resistance, or increased parasite virulence are some of the factors that favor the formation of a liver abscess. A liver abscess may be prevented even in the presence of an amebic hepatitis with intensive and prolonged treatment. Prevention and prophylaxis is the best cure.

When the abscess has developed, open surgical drainage with intense antiamebic treatment both pre- and postoperatively will cure the condition. Early open surgical drainage should be done when the patient continues toxic, when there is evidence of progressive liver damage, or when secondary infection occurs. There is no additional hazard to open drainage of these abscesses if the necessary precautions are taken.

Six patients with amebic liver abscess diagnosed preoperatively were treated with 5,7-dicloro-8-oxyquinaldine* by mouth; emetine hydrochloride subcutaneously; an antibiotic of the tetracycline series, and open surgical drainage. None of the patients died. All of the patients were discharged from the hospital 14 to 21 days after surgery. Immediately after open surgical drainage the patients noted a great clinical improvement.

Fig. 1.—Female. Note crescentic elevation of the midportion of the dome of the right leaf of the diaphragm and signs of right lower-lobe abscess with continuity into the liver substance.

Report of Cases

Case 1.—A woman aged 32 entered the hospital in January, 1952, complaining of a productive cough with hemoptysis, loss of weight, and anorexia of four months' duration. At the onset of the illness there had been some diarrhea, chills, and fever lasting about 10 days. Physical examination revealed increased breath sounds over both lung fields, pectoriloquy, and an increase in the area of liver dullness. The patient appeared acutely ill. The temperature was 39.7 C (103.5 F); pulse rate, 110. Laboratory findings were essentially normal except for a white cell count of 12,450 with 75% neutrophiles. The stools were negative. X-ray of the lungs showed a dense homogeneous shadow involving the right base from the hilum to the periphery between the 9th and 11th ribs. The impression of the radiologist was pulmonary tuberculosis or pulmonary abscess of undetermined origin. The sputum was negative for Bacillus tuberculosis. The patient was immediately placed on antibiotic therapy, bed rest, and supportive measures. Ten days after the original examinations the stools showed the presence of E. histolytica, as did the sputum. Two days later, a repeat x-ray showed a cavity in the center of the zone of infiltration. Intensive antiamebic medication was started, and the stools became negative in about one week. After two consecutive negative stools at 48-hour intervals, a

* Supplied by J. R. Geigy, S. A. (Geigy, Suisse).

laparotomy was performed. This revealed a large solitary abscess of the right lobe of the liver. The abscess was opened and aspirated of 600 cc. of a foul-smelling dark blackish-red pus that looked like chocolate sauce. Exploration of the abscess cavity revealed upward extension into the lower right chest through the diaphragm. A large Pezzer catheter was inserted into the lower right chest and brought out through a lateral stab wound; two other Pezzer catheters were placed in the abscess cavity, with two Penrose drains, and two other drains were placed beneath the liver border. The wound was closed in layers. Drainage was profuse for 72 hours, and the catheters were irrigated three times daily with an emetine solution, the patient receiving intensive antiamebic therapy during this time. Recovery was rapid, with cessation of drainage in about five days and gradual closing of the drainage and abscess sites, so that the patient was discharged from the hospital four weeks after surgery. She has regained her strength and weight and has remained in good health since that time.

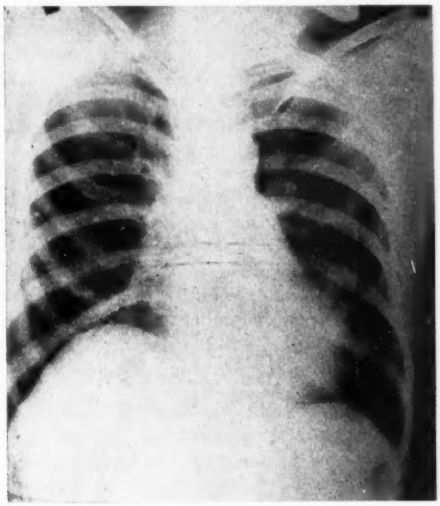

Fig. 2.—Male. Note crescentic-shaped elevation of the right dome of the diaphragm, with increased hepatic density and downward extension of the liver.

CASE 2.—A woman aged 27 entered the hospital in April, 1952, complaining of pain in the right upper abdominal quadrant, fever, and chills of one and one-half months' duration. There was also an abdominal mass that would increase in size during the periods of chills and fever but would diminish in size when these stopped. The mass was tender and painful at all times. There was anorexia, dyspepsia, loss of energy, loss of weight, and some nausea. There was no diarrhea, but the patient recalled having had amebiasis since 1950. Treatment had been sporadic and uncontrolled. Physical examination revealed a chronically ill woman with a subicteric tinge to the skin. The temperature and pulse were normal. The liver was palpable 4 fingersbreath below the costal margin. It was tender and painful. Liver dullness extended upward from 1 in. (2.5 cm.). Laboratory examination revealed a white cell count of 15,500, with 65% neutrophiles. The stools were positive on admission for E. histolytica. Flat plate of the abdomen revealed an increase in the normal abdominal shadows, with obliteration of the psoas shadow and an increase in the hepatic area. The impression was a subphrenic abscess. Three days after admission intense antiamebic treatment was started, and the patient was prepared for surgery in seven days. On laparotomy a large solitary abscess of the right lobe of the liver was found which contained 1400 cc. of a thick red-purple pus. It had a foul odor. Two large Pezzer catheters were inserted in the abscess cavity, and two Penrose drains, while the subhepatic area was also drained. The abdomen was closed in layers. Intense antiamebic therapy was continued and the abscess irrigated three times daily through the catheters. The patient was discharged from the hospital three weeks after open surgical drainage of the abscess and has remained symptom-free since that time.

CASE 3.—A girl aged 12 entered the hospital in October, 1952, complaining of recurrent fevers, hypogastric pain, an abdominal mass, and vague gastric disturbances of four months' duration. The patient appeared cachectic, wasted, and chronically ill. The temperature was of the recurrent type, with an afebrile phase lasting 72 to 96 hours. There was marked tenderness over the entire liver area, with an increase upward of the area of liver dullness. Laboratory examination revealed a white blood cell count of 22,800, with 85% neutrophiles. The stools were positive for E. histolytica on admission. Flat plate of the abdomen revealed a great increase in the density of the hepatic area which extended 2 in. (5 cm.) above the left paravertebral border to the level of the fourth lumbar vertebra. There was an irregular elevation of the right leaf of the diaphragm. The patient was immediately started on an intense antiamebic regimen. She was ready for surgery 14 days after admission. Exploratory laparotomy revealed a solitary right-lobed abscess containing about 1200 cc. of a dark red foul-smelling pus. The abscess and abdomen were drained as in the other cases and the wound closed. Therapy was continued, and the patient was discharged from the hospital in excellent condition three weeks after surgery.

CASE 4.—A man aged 29 entered the hospital in April, 1953, because of a productive cough, pain in the right chest, hemoptysis, and loss of weight

and energy of two months' duration. He had an attack of intestinal amebiasis six months prior to the present illness, and the stools had shown the parasite almost constantly since that time. One week prior to his hospitalization he had noticed pain and tenderness over the liver, a sense of fullness in the epigastrium, and some dyspepsia. The patient appeared ill. The temperature and pulse were normal on admission. Laboratory findings revealed a white cell count of 16,800, with 80% neutrophiles. The stools were positive for E. histolytica on admission. The sputum, which was foul-smelling, also revealed the parasite in large numbers. Chest x-ray revealed a hazy homogeneous shadow over the lower right and lower lobes, with elevation of the diaphragm on the same side. The hepatic shadow was enlarged downward and to the left. (Patient refused permission to use the photographs.) Intense antiamebic therapy was instituted, and the patient was ready for surgery in seven days. At laparotomy a solitary abscess of the right lobe was found, containing 1450 cc. of a thick blackish-red to purple pus. Drainage was as in the other cases. Recovery was rapid, and the patient was discharged from the hospital in three weeks.

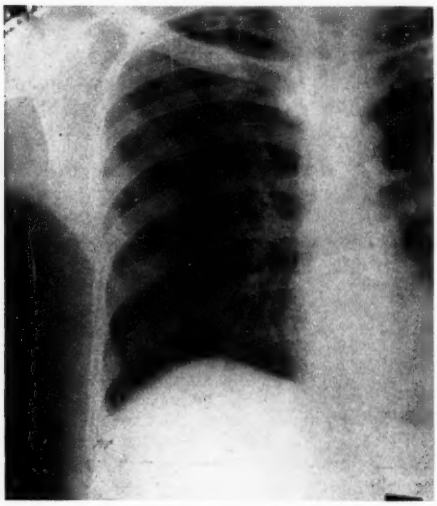

Fig. 3.—Male. Note crescentic-shaped elevation of the right dome of the diaphragm, with increased hepatic density.

CASE 5.—A man aged 55 entered the hospital in October, 1953, complaining of a mass in the right upper quadrant, intense pain over the liver, chills and fever, and vomiting of one month's duration. The illness had been preceded by a change in bowel habits, with diarrhea, tenesmus, and pain on defecation but no blood or mucus in the stool. The liver was palpable 2 fingersbreadth below the costal margin. The patient had had an attack of amebiasis as a child but received no treatment at any time. Laboratory examination revealed a white blood cell count of 17,500 cells, with 75% neutrophiles. The stools were positive on admission for E. histolytica in both trophozoite and cyst forms. An x-ray of the abdomen revealed elevation of the right dome of the diaphragm, with a great increase in the liver shadow. The patient was immediately subjected to the intense antiamebic regimen outlined before and was ready for surgery in 10 days. At laparotomy a large solitary abscess of the right lobe of the liver was found, containing 1200 cc. of a purplish-black to red stringy pus that contained E. histolytica trophozoites. Pezzer catheters were placed in the abscess cavity and Penrose drains in the subhepatic region, and the abdomen was closed. The patient responded well, and the treatment was continued for two weeks; he was discharged from the hospital in three weeks. His stools became parasite-free and have remained so to date.

CASE 6.—A man aged 43 entered the hospital in October, 1953, complaining of a painful swelling in the right upper quadrant, dyspepsia, anorexia, weakness, loss of weight, and moderate to mild diarrhea of one month's duration. Examination revealed a moderately ill patient with some difficulty in respiration. The abdomen was tender overall, but more marked over the liver area. The liver was palpable at the costal margin and was very tender. The pulse and temperature were normal. He had an attack of amebiasis in 1950, for which he received three courses of treatment at various intervals of one month each; another attack in 1951, with interrupted unsupervised treatment for two weeks; another attack in 1952, without treatment, and another attack in 1951, which was treated for one week. Laboratory findings revealed a white blood cell count of 15,000, with 65% neutrophiles. The stools were negative twice immediately after admission but became positive 72 hours later for E. histolytica. The patient was then placed on the intensive antiamebic regimen, and the first stool was negative in seven days. Laparotomy was performed seven days later. When the abdomen was opened, a large solitary abscess of the right lobe was found, containing 1850 cc. of a thick reddish-black foul-smelling pus. This was aspirated, and the abscess cavity was drained with three Pezzer catheters. The subhepatic area, foramen of Winslow, and retroduodenal areas were drained with Penrose drains. The abdomen was closed in layers. Postoperative treatment was continued, and the patient was discharged from the hospital 18 days after surgery, in good condition.

Box 313.

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The Radical Control of Postprostatectomy Hemorrhage

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While the problem of hemorrhage has been a major consideration in prostatic surgery for as long as that field of endeavor has existed, the urological surgeon has devised a number of effective methods which almost always lead to its successful management. Apart from direct ligation of bleeding vessels in open operative approaches, electrocoagulation, inflatable bags serving as tampons, and direct packing have all been utilized and proved invaluable.

The medical literature, on the other hand, contains numerous accounts of the employment of more radical measures to control other types of pelvic hemorrhage. These have principally dealt with uterine hemorrhage due to neoplastic disease or operative trauma; however, such measures have also been applied in controlling the blood loss from extensive bladder neoplasms. In these situations bilateral internal iliac artery ligation has been performed after failure of all other measures.

One decisive consideration attends all procedures in any part of the body in which a major artery is ligated for the control of hemorrhage. For always the operator must realize that he seeks by this attempt to diminish blood flow sufficiently to halt bleeding; yet he seeks also to maintain an adequate flow of oxygenated blood to assure viability of vital and adjacent parts. Hence, a balance is required of differing degrees of delicateness.

Although bilateral internal iliac artery ligation has been reported often enough to call attention to ischemic complications, if they in fact existed, there is virtually a complete absence of any such description in the literature. The pelvic viscera are known to have an excellent collateral arterial supply. Thus, the pelvic colon might be expected to be protected by anastomoses between the superior, middle, and inferior hemorrhoidal arteries. Likewise, the mid and lower urinary tract should be adequately served by the deep epigastric, the external pudendal, and perhaps even the spermatic arteries.

The necessary balance should then hinge only upon effecting adequate reduction of blood flow. The following case report is designed to demonstrate the value of this procedure in an extremely desperate situation recently encountered (the method not having been previously reported for use in this problem in the American literature). It was indeed a unique problem, for as mentioned previously, postprostatectomy hemorrhage of almost any magnitude is practically always controllable by conventional and less radical means.

Report of a Case

This 76-year-old man was admitted to the San Gorgonio Pass Hospital on Feb. 2, 1956. He had experienced increasing symptoms of prostatism for the past 20 years and had noted slight hematuria on two previous occasions. In the past three or four months the frequency, hesitancy, nocturia, and decrease of urinary stream had become very pronounced. One week before his admission, complete retention had necessitated the use of an indwelling catheter. Past history included bilateral varicose veins of the legs for 20 years, typhoid in 1903, hemoptysis leading to a year of sanatorium care in 1914, and bilateral mastoidectomy (1913 and 1914).

The positive physical findings were slight car-

Submitted for publication May 1, 1956.

diac enlargement, large bilateral varicose veins of the legs, and a marked and symmetrical enlargement of the prostate gland, which was smooth and rubbery. The vital signs were within normal limits.

The admission urinalysis disclosed 100 to 150 white blood cells and 8 to 10 red blood cells per high-power field. The hemogram was within normal limits.

On Feb. 6, 1956, at 9 a.m. suprapubic prostatectomy and bilateral vasectomy were performed with the patient under spinal anesthesia. The gland weighed 230 gm. The patient received a 500-cc. blood transfusion during the procedure. A No. 26 Foley catheter with a 75-cc. bag inflated was left in place, controlling bleeding; continuous irrigation was then established.

After surgery, active, bright red bleeding continued in large amounts through the urethral catheter and marked hypotension developed.

The patient was returned to the operating room at 12:10 p.m., and under endotracheal anesthesia induced with thiopental (Pentothal), succinylcholine (Anectine), and nitrous oxide—oxygen, multiple bleeding points in the operative field were coagulated through a resectoscope. After this procedure, however, bleeding and shock continued, and the patient could not be moved. From 2 p.m. until 2:03 p.m., there was no evidence of any cardiac beat; spontaneous resumption occurred at the latter time, although deep shock persisted. From 3:45 p.m. reasonable blood-pressure levels were maintained by continued use of levarterenol (Levophed) intravenously and blood transfusions. During this time there was a persistent, pulsatile flow of frank blood from the urethral catheter.

It was then decided that reoperation was mandatory as soon as adequate amounts of blood were available. Thus, at 7:15 p.m. the suprapubic incision was reopened and the bladder entered. Active arterial bleeding was encountered from myriad points in the bladder neck and prostatic urethra, with visualization being quite difficult. Many bleeding areas were ligated and sutured by means of a continuous bladder neck suture, but a vigorous arterial flow continued. The bladder had become edematous and friable making suture technically difficult. A last attempt at direct control was made by densely packing the prostatic bed. However, vigorous arterial flow persisted through the packing. There was no demonstrable capsular retraction, and it was felt that bleeding was coming from the vessels arising at the apex of the prostatic bed.

Bilateral ligation of the internal iliac arteries was therefore elected. The incision was extended rostrad, opening the peritoneal cavity. With the intestine packed away, the posterior parietal peritoneum was incised for short distances bilaterally. Each internal iliac artery was doubly ligated in continuity with medium nonabsorable surgical (silk) suture. The hemorrhage from the prostatic bed abruptly ceased, and after wound closure, the patient was returned to his room. A 5-cc. Foley catheter (No. 26) was placed in the bladder through the suprapubic wound, and a 30-cc. Foley catheter (No. 26) was left in place through the urethra. The total blood administered was 5500 cc.

Postoperatively the patient received a continuous intravenous drip of levarterenol, calcium, oxygen, a broad range of antibiotics, and continuous gastric suction. Urine volume was always adequate. He became oriented about 36 hours later, after which alertness progressively returned. Adequate blood pressures could be maintained without levarterenol after 72 hours. The Levin tube was removed when bowel sounds returned on the third day. On Feb. 13, the pack was removed in the operating room with the patient under meperidine (Demerol) analgesia, and no bleeding occurred. Ambulation was progressive after that time, and he was able to leave the hospital on the 12th postoperative day. Since then, he has progressed well, although rather slow healing of the suprapubic sinus was noted. There are at present no residual ill effects from the procedure.

Summary and Conclusions

A case of bilateral internal iliac artery ligation for control of otherwise uncontrollable postprostatectomy hemorrhage is reported. There were no ischemic or other sequelae from the procedure, and the control achieved was prompt and adequate.

Although this relatively simple technique has been usefully employed for other major pelvic hemorrhages, it has not to our knowledge been employed in this problem before. It is recommended as an excellent expedient for the urologist when his usual means are unavailing.

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Neurilemomas of the Vagus Nerve in the Neck

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Neoplasms of the peripheral nerves are rather common, but tumors involving either the sheath or ganglion of the vagus nerve in the neck are so rare that each case is worthy of record. The well-known neurofibromas of Recklinghausen's disease have been found to arise from the vagus nerve in both the cervical and the thoracic region. But another, different, specific tumor has been found in the cervical vagus, distinct from the classical neurofibroma. This specific well-differentiated tumor, which develops within the nerve sheath, was first described histologically by Verocay in 1908[1] and called by him "neurinoma" in a report in 1910.[2] Since then, the names perineurial fibroblastoma,[3] schwannoma, neurilemoma,[4] peripheral glioma, and neurilemnoma [5] have been used frequently.

Histogenesis

The long controversy over the exact histogenesis of these tumors has produced this varied terminology. One group of investigators, led by Penfield,[6] contends that the tumor is of fibroblastic origin and, therefore, a mesenchymal neoplasm. They argue that the tumor cells are fibroblasts morphologically and only fibroblasts can produce collagen found in the tumor. However, there is considerable evidence to substantiate the schwannian, or ectodermal, theory. This theory contends that the tumor arises from the cells of Schwann and is an ectodermal neoplasm. Masson [7] and Murray and Stout [8] demonstrated by tissue cultures that the cells of these nerve sheath tumors are morphologically and physiologically similar to the cells of Schwann. Murray and Stout have cultivated the tumor in vitro and have demonstrated the derivation of reticulum fibers from the cells of Schwann. The bulk of evidence, therefore, appears strongly to favor the schwannian theory. But the difference of opinion exists. And, since it is generally agreed that this is a tumor of neurilemma, Stout's contribution of "neurilemoma"[4] appears reasonably specific.

Submitted for publication April 20, 1956.

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History

As mentioned previously, this specific tumor, composed of highly differentiated tissue so characteristic of the nerve sheath within which it develops, was first adequately described Verocay in 1908.[1] Since then, these nerve sheath tumors have been found to arise from nerves in any part of the body. However, they are more commonly confined to certain areas. These neoplasms are more numerous in the extremities but are found with considerable frequency in the neck, with its multiplicity of cranial nerves, sympathetic nerves, and branches of the brachial plexus. Less frequently, the larynx, pharynx, tongue, lip, palate, floor of the mouth, maxillary sinus, eyelids, orbit, salivary gland, thorax, abdominal cavity, and skin have been involved. We are concerned here primarily with isolated nerve sheath tumors of the vagus nerve in the neck. These are exceedingly rare tumors.

Individual cases have appeared in the literature by Sekiguchi and Oije in 1926,[9] Cutler and Gross in 1936,[10] Murley in 1948,[11] Paul in 1949,[12] and Parnes in 1955.[13] Ehrlich and Martin [14] reported two cases in 1943. Stout,[4] in 1935, reported a case of paraganglioma of the ganglion nodo-

sum of the vagus nerve. Another somewhat different type of tumor, called a vagal-body tumor, was presented by Burman, in 1955.[15] Therefore, it is apparent that true nerve sheath tumors of the cervical vagus are very rare and that all new cases are of considerable interest.

Pathology

Grossly, these tumors are encapsulated and either globular or fusiform in shape. The external surface is smooth and has a gray or yellowish-gray appearance. The consistency is soft and sometimes fluctuant. This characteristic is explained by the cystic degeneration that this tumor usually undergoes. However, the growth may be firm and fibrous. The size is variable, ranging from 1.5 cm. to 10 cm. The cut surface is glistening and reveals a multiplicity of patterns.[14] Most frequently irregular, mottled areas are seen, ranging from pink to yellow to pearl gray. The central portion of the tumor is almost always necrotic. Hemorrhages are frequently scattered throughout, especially beneath the capsule. Degeneration cysts, which may vary markedly in size, are filled with fluid of various shades of color from straw to red and brown. Often there are small but visible blood vessels dotting the surface.

For many years, it has been customary to divide the histologic appearance of this nerve sheath tumor into the type A and type B tissues of Antoni.[16] Type A is characterized by a reticulum of fine long wavy fibers passing between the cells. The cells and their nuclei are elongated, and cytoplasmic processes stream out to form a network. The intercellular fibers are arranged in a parallel manner, while the cell nuclei are lined up at the opposite end of the fibers. This palisading, or the arrangement of the cell nuclei in parallel rows, "like nuclei on parade," is characteristic (Fig. 1). Areas of fibrosis, necrosis, and hemorrhage are commonly scattered throughout. Thrombosis within thick-walled blood vessels is not uncommon. This necrotizing process produces areas devoid of cells or fibers, which then become cystic. No axis cylinders are seen. Mitoses are rare or absent.

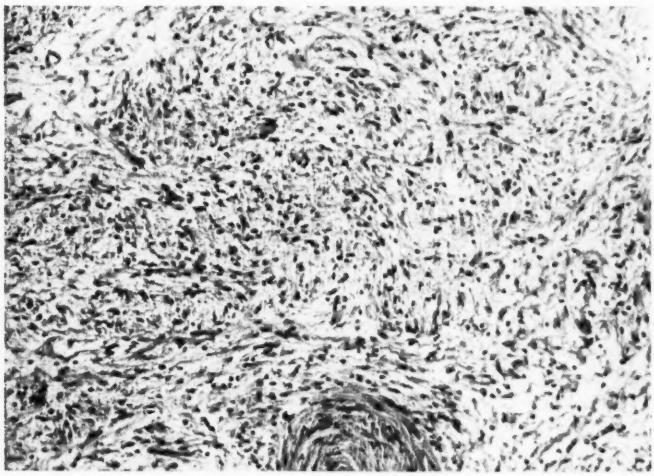

Fig. 1.—Antoni type A tissue, revealing dense elongated fibers with nuclear palisading and arterial thrombosis. Hematoxylin and eosin; reduced from mag. ×194.

In the type B tissue no orderly arrangement of cells and fibers exists. There is no palisading of nuclei. This type is characterized by being very loose-textured, owing to intercellular fluid, which separates the cells and fibers, and often to the collection of fluid degeneration products into microscopic rounded, cystic areas. This is the so-called microcystic degeneration seen in type B (Fig. 2). Collagen bands are rarely found. It is the absence of collagen bands

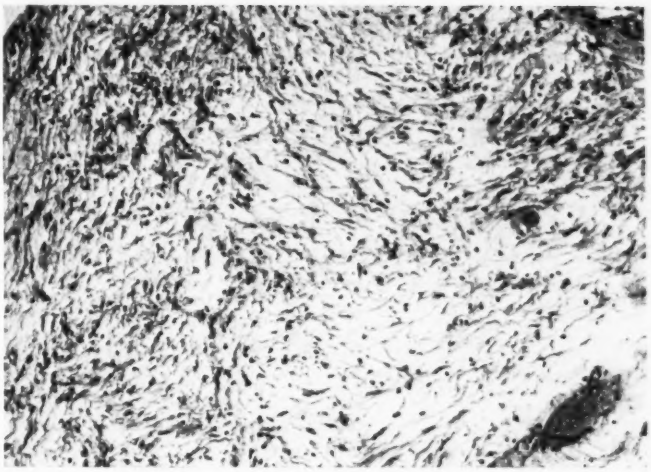

Fig. 2.—Antoni type B tissue, showing loose texture, no definite cellular arrangement, and presence of microcystic degeneration. Hematoxylin and eosin; reduced from mag. × 194.

and of axis cylinders and the presence of microcystic degeneration which cause this type B tissue to differ from the tissue composing the usual neurofibroma of Recklinghausen. Masson [7] follows Antoni in stating that the type B tissue is a degeneration form of the type A.

The ordinary neurofibroma consists of a diffuse and rich supply of nerve fibers intermixed with the connective tissue overgrowth. The nerve fibers are either medullated or nonmedullated.

Clinical Manifestations

The fact that these tumors have frequently been incorrectly diagnosed preoperatively indicates that symptoms are few and variable and not characteristic. The only constant presenting complaint is that of a mass or localized swelling in the neck. The mass is often soft and occasionally presents a cystic consistency. Like carotid-body tumors, the neurilemoma of the vagus nerve in the neck is partially fixed and moves more freely from side to side than in a vertical direction. The mass does not pulsate but may transmit pulsations from the adjacent carotid artery.

If the mass has attained large proportions over a long period of time, there may be some dysphagia from local impingement upon the esophagus or pharynx. Pain, when present (rarely), is mild and of aching character. Occasionally symptoms referrable to vagal irritation are present and are manifested by coughing, hoarseness, or mild tachycardia. It is conceivable that malignant tumors of the vagus nerve would produce more symptoms of vagal irritation with invasion and/or destruction of the nerve fibers.

Furrer and Fox, in 1940,[18] reported a case of perineural fibrosarcoma of the left vagus in the neck. Stout in 1935 presented, in his large group of cases of nerve sheath tumors, a case of malignant paraganglioma of the ganglion nodosum of the vagus nerve. Therefore, malignant tumors of the vagus nerve are possible. However, the specific tumors under discussion are benign, and there is no indication that such a tumor undergoes malignant change.

Neurilemomas of the vagus nerve may conceivably appear at any age, but they are most commonly found from the third through the fifth decades. Both sexes are equally affected. The right side of the neck is as often involved as the left, though our three cases possessed tumors on the right. These tumors may occur with similar tumors in other locations anywhere in the body and may be present as part of the manifestations of the Recklinghausen's disease.

Report of Cases

The following cases of neurilemoma of the vagus nerve in the neck were seen and treated at Duke Hospital. All of our cases were benign, and there has been no evidence of recurrence following surgical excision.

CASE 1.—A 39-year-old man was admitted because of multiple discrete masses of the right foot, thigh, and neck. The mass in the foot had been present 12 years, while the others were of 2½ years' duration. All lesions were asymptomatic except for slight gradual increase in size. The patient was in good general health, without other lesions. Physical examination revealed a 3×3×2 cm. moderately firm, partially fixed, nontender mass presenting beneath the medial margin of the midportion of the right sternocleidomastoid muscle. No pharyngeal or intraoral lesions were present. The masses in the right thigh and right lateral foot measured 3×3×1 cm. and 2×2×2 cm., respectively, and were similar to the neck lesion on examination. No pigmented nevi were found. The remainder of the physical examination was essentially normal. Routine laboratory studies and an x-ray of the chest were normal. The clinical impression was multiple neurofibromatosis.

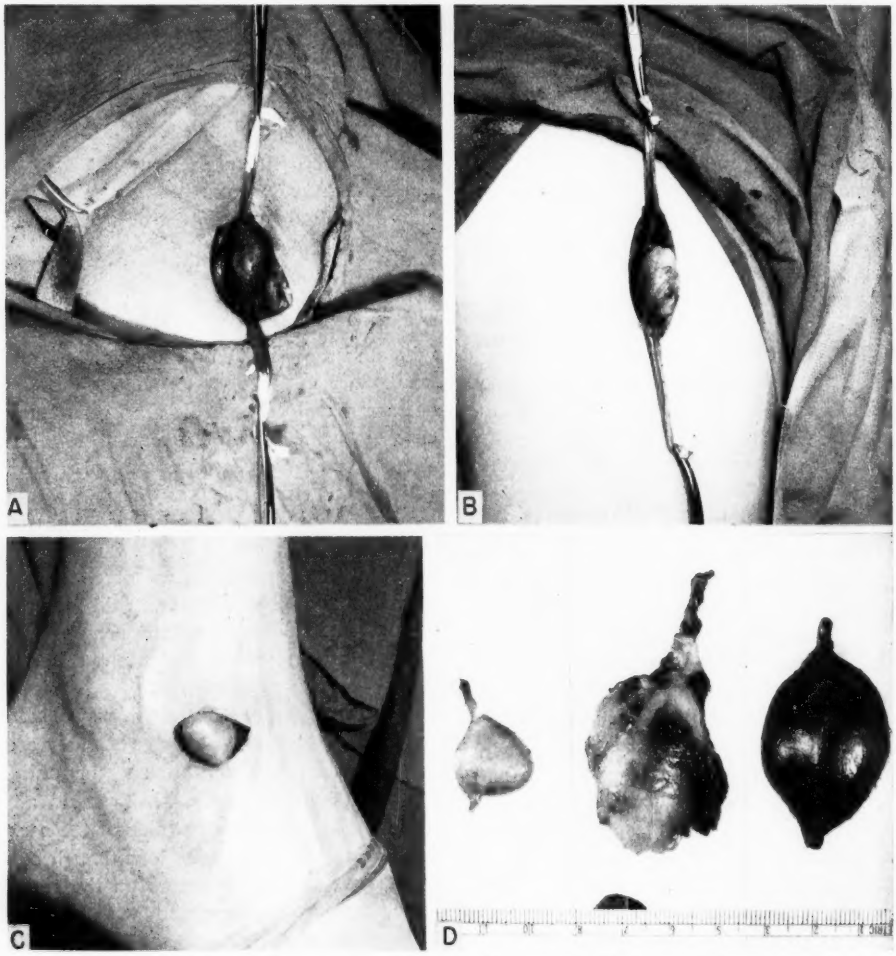

Fig. 3.—Multiple neurilemomas from Case 1. *A*, tumor of right cervical vagus nerve seen through operative incision, with tape around proximal and distal nerve segments. *B*, tumor of lateral aspect of right thigh. *C*, similar tumor of right ankle. *D*, gross appearance and comparison of the three neurilemomas.

After complete evaluation the patient was taken to the operating room, where, under general anesthesia, the three tumors were removed (Fig. 3). The mass in the neck was exposed through an incision following the transverse skin lines over the sternocleidomastoid muscle. The carotid sheath was opened and revealed the internal jugular vein to lie directly over the mass. This was dissected free, and the fusiform tumor was found to involve the vagus nerve. Since it was impossible to separate the tumor from the nerve fibers, the nerve was injected with 2% procaine above and below the mass and the lesion was completely excised, along with a proximal and distal segment of normal-appearing vagus nerve. Owing to the large size of the tumor, primary nerve suture was impossible. The wound was closed in layers with 00000 nonabsorbable surgical (silk) sutures. The two remaining tumors were excised in a similar manner. The diagramatic appearance and location of the cervical tumor in this case are illustrated in Figure 4.

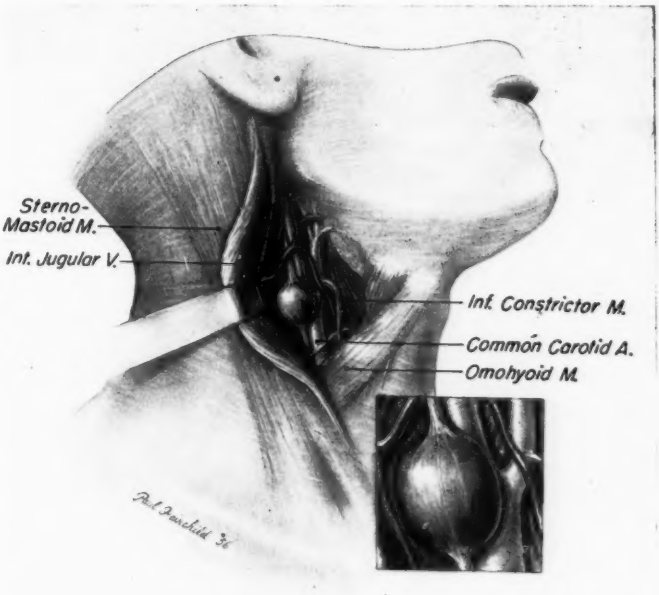

Fig. 4. — Diagramatic representation of typical appearance and location of fusiform neurilemoma of the right vagus nerve in the neck as found in Case 1.

All three lesions had a similar microscopic appearance. To the periphery of the thick connective tissue capsules were attached nerve fibers which did not enter the main tumor mass. The tumors were composed of loose reticular tissue mixed with parallel sweeping strands of narrow, elongated cells showing nuclear palisading. This was classified as Antoni type A. Moderate vascularity was present. No axis cylinders could be identified (Fig. 1).

The patient's postoperative course was complicated only by slight hoarseness of voice due to paralysis of the right vocal cord. Frequent follow-up examinations revealed no recurrence or new lesions, and the slight hoarseness was somewhat improved.

CASE 2.—A 24-year-old white man was admitted because of a soft asymptomatic progressively enlarging mass in the right upper neck on the right side of six months' duration. The mass had been partially excised elsewhere one month prior to admission, resulting in marked hoarseness of voice immediately postoperatively. The biopsy diagnosis was possible vagus nerve tumor. Otherwise, the patient's general health was excellent. Physical examination at the time of admission revealed a well-developed well-nourished white man appearing well but speaking in a low-pitched voice, unable to increase the voice volume above normal conversational range. There was a definite firm tumor mass in the upper neck anterior to the right sternocleidomastoid muscle surrounded by a wide area of induration of the skin and subcutaneous tissues. The skin overlying the mass contained a well-healed 4 cm. transverse incision. The entire tumor mass was fixed and nontender. Indirect laryn-

goscopy revealed complete paralysis of the right vocal cord with some hyperemia and edema of both vocal cords. No other lesions were noted on thorough examination. Hemoglobin, white blood cell count, differential count, and urinalysis were normal. Radiologic examination of the chest and cervical spine revealed no abnormality. The clinical diagnosis was possible neurofibroma of the right vagus nerve.

The mass in the neck was explored under general anesthesia through a long transverse neck incision overlying the main portion of the tumor. The carotid artery and jugular vein were dissected free from a dense mass of thick scar tissue. The vagus nerve was identified imbedded in the scar tissue, with the portion of the nerve below the tumor mass being completely divided. The main tumor mass was found to be well encapsulated, partially cystic, and pale yellow. By sharp and blunt dissection, the entire tumor was removed in addition to a short segment of proximal vagus nerve near the jugular foramen. The wounds were closed in layers, with use of interrupted 0000 silk sutures. Microscopically, this tumor had the same appearance of that in Case 1. Immediately postoperatively, the patient was found to have a partial Horner syndrome on the right, with ptosis of the upper lid and constriction of the right pupil. Hoarseness of the voice was persistent. At the time of discharge, on the seventh postoperative day, the wound was well healed but hoarseness was still present. The ptosis of the right upper eyelid was improved. Follow-up examinations revealed no recurrence or new lesions. The Horner syndrome had disappeared, but hoarseness of voice was persistent.

Case 3.—A 22-year-old white man was admitted to Duke Hospital for the evaluation and treatment of a solitary asymptomatic gradually enlarging mass in the right neck of three years' duration. The patient first noticed the lesion while shaving, at that time. He had always been in good health, and no other abnormality was apparent. Physical examination revealed only the presence of a large mass at the angle of the mandible on the right beneath the sternocleidomastoid muscle, protruding from its posterior margin. The lesion was slightly soft, nontender, and freely movable and measured approximately 8×4 cm. Routine laboratory studies plus roentgenologic examinations of the neck and chest were normal. The clinical diagnosis was branchial cleft cyst.

Under general anesthesia, the tumor mass was exposed through a 6 cm. oblique incision over the mass and parallel to the inferior border of the mandible. The lesion consisted of a 7×4 cm. globular yellow-white semisolid and partially cystic tumor lying on the carotid vessels at the bifurcation. The vagus nerve was seen to enter the top of the tumor and pass inferiorly along its lateral surface. The entire tumor, accompanied by a short segment of nerve on either side, was excised. Primary vagus nerve suture was not possible.

Pathologically, the tumor possessed a thick fibrous capsule, with the capsule being rather translucent, edematous, soft, and greenish-yellow. Microscopically, the center contained cystic spaces partially filled with red blood cells and hyalin debris. The main body of the tumor was loose-textured and contained a large amount of intercellular fluid between the elongated fibers.

The entire structure exhibited the so-called microcystic degeneration described as Antoni type B (Fig. 2). Mitoses were absent. The postoperative course was uneventful except for immediate hoarseness of voice due to paralysis of the right vocal cord. Recent examinations find the patient free of recurrence, but impairment of voice has continued.

Diagnosis and Differential Diagnosis

It is apparent from the lack of characteristic symptoms and signs produced by these tumors that diagnosis is rarely ever made preoperatively. As was true in our cases, the diagnosis of a benign nerve sheath tumor was made at the time of operation or from previous biopsy before definitive surgery was performed. In the usual case of neurilemoma, the long duration of the tumor with slow progression, the absence of any intraoral or pharyngeal lesion which might produce cervical metastasis, and the discrete soft movable character of the mass should lead the astute examiner to a tentative diagnosis of a benign primary neoplasm in the neck. No one can ascertain further the exact type of tumor present from the presenting clinical manifestations. The varieties of benign, soft tissue tumors in the neck are extremely numerous, and definite clinical diagnosis is impossible. Some of the lesions that would necessarily be considered in the differential diagnosis are lipoma, cystic hygroma, thyroid adenoma, submaxillary gland tumor, cervical node metastasis, lymphosarcoma, carotid-body tumor, aneurism, branchial cleft cyst, sabaceous cyst, tuberculous lymph node, and parotid tumor.

Some surgeons have advocated preoperative needle aspiration biopsy.[14] This proce-

dure may be of special value in those tumors which present into the retropharyngeal and retrotonsillar fossa, where operative intervention is hazardous.

Treatment

The accepted treatment of these nerve sheath tumors of the vagus nerve is surgical excision. Frozen section at the time of operation can give the surgeon definite diagnosis and determine whether the tumor is benign, potentially malignant, or a true malignant neoplasm. At the time of surgery, these tumors are situated beneath the upper one-third of the sternocleidomastoid muscle and are usually anterior to the carotid vessels (Fig. 4). They are not usually attached to surrounding structures. In the saccular tumors the nerve fibers are pushed to one side and are found together in this location adjacent to the tumor mass. In the fusiform type the tumor may be found inside the main nerve trunk, with several or all of the branches spread over the tumor surface in considerable disarray.[4] The nerve bundles, themselves, are never found inside the tumor capsule. But irregular slender tangled neurites usually pass into the superficial part of the tumor lying immediately beneath the capsule. Both arrangements make it extremely difficult to perform an extracapsular removal of the tumor without producing permanent damage to the main nerve trunk. While an intracapsular "shelling-out" of the tumor should not produce nerve damage, this technique could conceivably lead to a high rate of recurrence. Therefore, many of the cases reported have been treated by total excision of the tumor mass in continuity with a small segment of proximal and distal vagus nerve. Primary nerve suture should be attempted when possible. The division or excision of a single vagus nerve in the neck produces transient tachycardia and hoarseness and diminishes voice volume due to paralysis of the ipsilateral vocal cord. There is no interference with the function of the vagus plexus and the secretion of gastric hydrochloric acid. Bruckschwaiger, in 1947,[18] reported a case of cardiac arrest occurring immediately after interruption of a single vagus nerve in the neck. But this is the only such incident on record.

Since partial voice loss is a significant disability, the removal of benign neurilemomas should be accomplished with as little damage as possible to the main vagus trunk. There has never been an instance of malignant change in this type of tumor. Potentially malignant lesions, such as occur in some patients with Recklinghausen's disease, should be excised with a normal segment of adjacent nerve, followed by neurorrhaphy when possible. Naturally, fibrosarcomas and neurofibrosarcomas should be widely excised, with all evidence of local extension located and removed. There is no place for roentgen therapy in the treatment of neurilemomas, since all tumors of nerve sheath origin are highly radioresistant. Small doses of irradiation produce no retardation of tumor growth, and larger doses produce considerable destruction of the adjacent normal tissues.

Prognosis

All cases of neurilemoma of the cervical vagus treated by surgical excision have been cured, and follow-up examinations revealed no recurrences. Paul[12] does not mention the ultimate result from his intracapsular removal of such a tumor. Sarcomatous lesions of the vagus have the same grave sequelae as similar tumors elsewhere in the body.

Comment

The term neurilemoma is probably the most specific name for the benign type of nerve sheath tumor first described by Verocay in 1908. The best evidence reveals that this tumor arises from the cells of the sheath of Schwann. Neurilemomas of the vagus nerve in the neck are exceedingly rare, and each case is worthy of record.

Summary and Conclusions

Neurilemomas of the cervical vagus nerve are benign and produce no characteristic signs or symptoms. They are best treated by local excision, with care taken to preserve the nerve trunk when possible. Section of the nerve results in unilateral vocal cord paralysis without effect on gastric motility and secretion. Surgical removal of these tumors results in complete cure.

Gross and microscopic characteristics of the tumor are discussed. Case reports of three neurilemomas are presented and added to the small number of such cases found in the literature.

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Islet-Cell Adenoma

Report of a Case with a Brief Review of Diagnostic Criteria

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I. Introduction

Spontaneous hyperinsulinism due to islet-cell tumors, while not a common condition, is one of which the medical profession is becoming increasingly aware, due to its dramatic symptomatology and the complete cure that may be effected by operative removal.

The typical symptom-complex was reported by Harris,[1] in 1924, the first surgical proof of hyperinsulinism by the Mayo Clinic,[2] in 1927, and the first surgical cures by Howland,[3] in 1929, and Cushing,[4] in 1930. The medical and surgical aspects have been extensively reviewed (Crain and Thorn [1949],[5] Lopez-Kruger and Dockerty [1947],[6] Howard, Moss, and Rhoads [1950].[7])

It is not proposed to review the multiplicity of causes of spontaneous hypoglycemia, of which some 25-30 have been listed by Conn.[8] However, it is well to note that over 80% of the cases are caused by (*a*) functional hypoglycemia, (*b*) organic hyperinsulinism, and (*c*) hepatogenic hypoglycemia.

Submitted for publication Jan. 23, 1956.

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II. Diagnosis

The diagnostic criteria that have been used in the past are as follows:

1. Clinical
   - (*a*) Hypoglycemic episodes progressive in frequency and severity
   - (*b*) Progressive neurologic symptoms (almost every clinical neurological symptom, diffuse or local, has been described in hypoglycemia)
   - (*c*) Prebreakfast attacks
   - (*d*) Attacks if meals are omitted
   - (*e*) Obesity (in more than 50% of reported cases)
   - (*f*) Relief of symptomatology following glucose administration
   - (*g*) Response to a high protein, low carbohydrate diet
2. Laboratory [9]
   - (*a*) Repeated low fasting blood sugars (less than 50 mg. per 100 cc., Folin-Wu method)
   - (*b*) Low blood sugar and/or symptoms after a 24-hour fast
   - (*c*) Abnormal glucose tolerance test
   - (*d*) Abnormal insulin tolerance test
   - (*e*) Abnormal epinephrine tolerance test
   - (*f*) Liver battery
   - (*g*) Assessment of pituitary-adrenal axis
   - (*h*) Electroencephalographic findings [10]

Report of a Case

On June 24, 1954, a 62-year-old white woman was admitted to the Boston City Hospital because of recurrent episodes of confusion. She had first been seen at Boston City Hospital in 1949 because of a flaccid quadriplegia lasting 12 hours. This had resolved itself spontaneously and left no residual findings. Complete neurological studies at that time demonstrated no specific disease.

Blood sugar on entry at that time was 72 mg. per 100 cc. and a fasting blood sugar, 70 mg. per 100 cc. She weighed 130 lb. The patient was discharged asymptomatic to be followed in the Neurologic Clinic, but she was not seen again until the current admission.

Present history revealed that since her discharge there had occurred monthly episodes of confusion, disorientation, and odd behavior. These attacks progressed in frequency and severity until they occurred two to three times per week during the six months prior to admission. They lasted 15 minutes to 1 hour and were associated with bizarre activity. The patient was unaware of many of these episodes but did note that several followed ingestion of bakery products or prolonged periods without food. No relationship to exercise was noted. No convulsions or loss of bladder function were ever described. On the morning of admission the patient was found sitting on the floor beside her bed. She was markedly confused and negativistic and was therefore admitted to the hospital.

System review and family history were noncontributory. The physical examination was within normal limits. The patient was described as having dull affect and a poor memory. Laboratory findings revealed a negative urinalysis. The hematocrit was 44%, WBC 9350 per cubic millimeter with a normal differential, and the blood urea nitrogen 13 mg. per 100 cc. Sulfobromophthalein (Bromsulphalein) test showed 0% retention after 45 minutes. The cephalin flocculation was 1+ in 24 hours and thymol turbidity, 0. Serum proteins were 6.3 gm. per 100 cc.; the formal gel, 0; urine urobilinogen, 0, and icteric index, 0. Lumbar puncture revealed clear colorless fluid with an initial pressure of 150 mm. water, normal dynamics, 0 cells, negative Pandy test, total protein 26 mg. per 100 cc., sugar 38 mg. per 100 cc., chloride 704 mg. per 100 cc., colloidal gold 0011110000, and Wasserman negative, smear and culture negative. Chest x-ray was negative. Skull films revealed a density consistent with an old calcified subdural hematoma. Electroencephalogram demonstrated continuous high-voltage 4-per-second delta activity in all areas. One seizure was noted involving the right leg, with concurrent rotation of the eyes to the right. During this attack, high voltage, bifrontal delta, and some spike activity were seen. Fasting blood sugars were 55 and 64 mg. per 100 cc. (Folin-Wu method).

One week after admission, she had a prolonged episode of unresponsiveness associated with hyperreflexia, bilaterally positive Babinskis, but no focal signs. Two blood sugars were obtained during this episode and were reported as 33 and 15 mg. per 100 cc. With the administration of intravenous dextrose symptoms disappeared, and the patient was responsive within five minutes. Ten days after admission, the patient had a six-hour oral glucose-tolerance test (100 gm. of glucose, orally, venous blood, true blood-sugar method), which revealed the following: Fasting, 56 mg. per 100 cc.; one-half hour, 124; one hour, 123; two hours, 90; three hours, 82; four hours, 59; five hours, 50; six hours, 39. This was followed several days later by a 24-hour fast with the following results: 13 hours, 33 mg. per 100 cc.; 18 hours, 23 (patient drowsy); 21 hours, 15; 24 hours, 11 (patient unresponsive). Intravenous dextrose was given, and patient responded immediately.

During her 24-hour fast she progressed through stages of confusion, drowsiness, and semistupor. Blood sugars were markedly diminished, and again clinical response was immediate following the intravenous administration of dextrose.

The patient was transferred to a surgical service with a preoperative diagnosis of islet-cell adenoma. On July 16, 1954, under endotracheal cyclopropane anesthesia, abdominal exploration was performed. There was no gross abnormality of liver, spleen, kidneys, stomach, or large or small bowel. The anterior surfaces of the head and body of the pancreas were negative. The duodenum was mobilized and the pancreatic head found to be grossly normal to inspection and palpation. The pancreas was next mobilized from the retroperitoneal structures along the inferior margin of the body and tail. A discrete firm mass of tissue measuring approximately 1.5 cm. in largest diameter could be palpated at the inferior margin of the tail. The tumor mass and tail of pancreas were resected. Examination of the remainder of the abdomen including large and small bowel disclosed no aberrant pancreatic tissue. Immediately preoperatively, during the entire operative procedure, and postoperatively the patient was maintained on a slow intravenous infusion of 5% dextrose and water. She was returned to the ward after the three-hour surgical procedure. Subsequently, all blood sugar determinations were normal, and the patient was aglycosuric. There were no further symptoms, and she was discharged on the ninth hospital day.

The resected tumor mass on section appeared to be well encapsulated and consisted of firm yellow-grey tissue with some hemorrhagic discoloration. Microscopic diagnosis was benign islet cell adenoma of the pancreas.

The patient has been seen six times since discharge (14-month follow-up) and has been entirely asymptomatic. Blood sugars have ranged from 64 to 86 (Somogyi-Nelson). Weight has been maintained at 105 lb., and no special diet has been necessary. Her average calculated food intake is 1200-1700 Cal.

Comment

In the diagnosis of islet-cell adenoma, although multiple clinical and laboratory tests may be applied, it is evident that no single reliable criterion exists. Repeated fasting blood sugars should be drawn. If Whipple's triad is present, (*a*) low blood sugar of less than 50 mg. per 100 cc., (*b*) symptoms of hypoglycemia, (*c*) relief with dextrose, there is presumptive evidence of an islet-cell tumor. Blood sugars should be drawn, if possible, at the onset of an attack, for if a convulsion occurs the blood sugar may be normal or elevated. Kornfeld [10] has stated that since hypoglycemic episodes develop in different patients at different blood sugar levels, the electroencephalogram may be useful as a correlative tool.

The glucose tolerance test is quite variable in the diagnosis of islet-cell tumors and the insulin tolerance and epinephrine tolerance of no value.* In some hands [11] the most reliable criterion has been the 24-hour fast—which in the aforementioned case dramatically demonstrated a progressive increase in symptoms correlated with a progressive fall in blood sugar. Additional tests used in evaluation of a patient with hypoglycemic symptoms include (*a*) liver battery to rule out hepatic malfunction and (*b*) tests of pituitary-adrenal axis to rule out hypopituitarism or Addison's disease. The response of the patient to a high-protein-low-carbohydrate diet is important to rule out functional hypoglycemia.

The present case demonstrated classical clinical and laboratory evidence of islet-cell tumor. Early surgical exploration was felt to be important because of the severity of the acute hypoglycemic attacks, because prolonged hyperinsulinism may result in mental deterioration and because of the high incidence of malignancy in islet-cell tumors. Since multiple adenomas are present in an appreciable number of cases, a thorough search for additional pathology was undertaken. This included mobilization of the duodenum and head of pancreas as well as the body and tail. The existence of a single adenoma in this case has been substantiated by the continued absence of symptoms postoperatively and the clinical evidence of normal glucose metabolism.

* References 5 and 9.

Summary

A case report of an islet-cell adenoma diagnosed preoperatively and successfully removed at surgery is presented. The diagnostic aspects are discussed, and it is pointed out that no single reliable criterion of diagnosis exists.

Dr. David Hurwitz, Chief, Diabetes Service, and Dr. Charles Lund, Chief, 5th Surgical Service, Boston City Hospital, aided in the management of the patient.

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Experience with Corticotropin and Corticosteroids in Severe Peritonitis

GEORGE C. HENEGAR, M.D.
ARTHUR J. HUNNICUTT, M.D.
and
LAURANCE W. KINSELL, M.D., Oakland, Calif.

It is generally recognized that the patient with an adrenocortical insufficiency has a poor tolerance to infection, even of a minor nature. It is also recognized that an overwhelming sepsis may produce a relative adrenal insufficiency. With the isolation and development of the adrenocorticotropic hormone of the pituitary and the various steroids of the adrenal cortex, an impetus was given to the study of the effects of these hormones on patients with severely toxic states.* Kass, Ingbar, and Finland showed that the course of a severe penumococcus pneumonia could be altered by the use of hormones alone.[7] These experiences by others led to the use of corticotropin in the case of a child who was severely toxic from a generalized peritonitis. The changes produced in this child were striking. Within 24 hours, the patient who had been moribund was clinically less toxic, had active peristalsis in contrast to a previously silent abdomen, and appeared well in spite of some persistent elevation of temperature (Fig. 1).[9] He was treated in a conservative fashion until his 20th hospital day. At that time the patient was explored and an appendectomy was carried out. A gangrenous appendix with a periappendiceal abscess was found. The patient was treated postoperatively with a blood transfusion and

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This work has been supported in part by grants from the Armour Laboratories; Merck and Company, Inc.; Schering Corporation; Pfizer Laboratories, Division of Charles Pfizer and Company, Inc., and the Upjohn Company. Armour Laboratories furnished supplies of corticotropin; Merck and Company, Inc., supplies of cortisone, hydrocortisone, and hydrocortisone hemisuccinate, and Upjohn Company, hydrocortisone hemisuccinate.

* References 1-6.

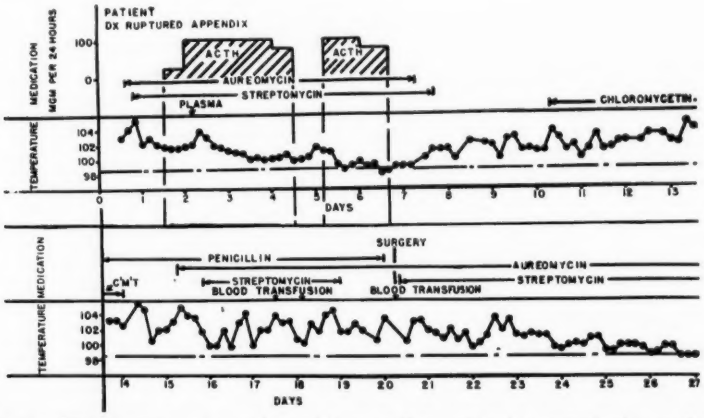

Fig. 1.—Clinical course of a patient with generalized peritonitis treated with corticotropin and antibiotics (Reference 9).

antibiotics. He was dismissed from the hospital on the sixth postoperative day.

The experience gained in the treatment of this first patient led to the rigid adherence to the principle of carrying out this type of treatment only when definitive surgical intervention is planned. This surgery is carried out in spite of apparent clinical improvement.

The basic principle behind the therapy of an acute overwhelming infection with adrenocorticotropic hormone and the adrenocortical steroid hormones is based on the hypothesis that these hormones block the toxic effect on the body cells, while the antibiotics and chemotherapeutic agents produce their growth-inhibiting effect directly upon the multiplying organisms. The exact mechanism for this toxin blocking effect is not known. At least three mechanisms can be considered:

1. An increased adsorption of toxins, perhaps by the materials released from lysed monocytes, lymphocytes, and eosinophiles.
2. A blockade at the level of the cell membrane, preventing the entry of the toxins into the cells.
3. A direct protective action upon the intracellular enzyme systems.

The course of treatment in these patients is to use the antibiotic drugs as inhibitors of the infectious organism and to operate as soon as it is considered safe to carry out an operative procedure in a severely ill patient. The cortical steroid drugs and the corticotropin (ACTH) are used to combat the systemic toxic effect and, in a sense, to permit one to "buy time" while the antibiotic drugs are producing their effect. As a result of our experience, we now have an organized program for combined hormonal, antibiotic, and surgical therapy. Immediately upon decision to use the hormones, the patient is given 100 mg. of hydrocortisone intravenously in 500 cc. of 5% dextrose in water. This is administered at the rate of 250 cc. per hour. At the same time 40 units of corticotropin are placed in the same intravenous solution. If the patient is an infant or if he is at the other age extreme in which fluids may create a problem, we now use hydrocortisone hemisuccinate; this can be given directly into the vein in 2 cc. of aqueous solution. This creates an identical rapid effect when compared with that of intravenous hydrocortisone. At the same time the patients are also started on a program of intramuscular cortisone acetate starting with 300 mg. a day in divided doses and declining in a step-wise fashion. Intramuscular corticotropin is given, decreasing it in a step-wise fashion also. The course of treatment is so outlined that the corticotropin continues for at least two days longer than the cortisone. The antibiotics are continued for at least one week following the discontinuation of the hormonal therapy (Fig. 2).

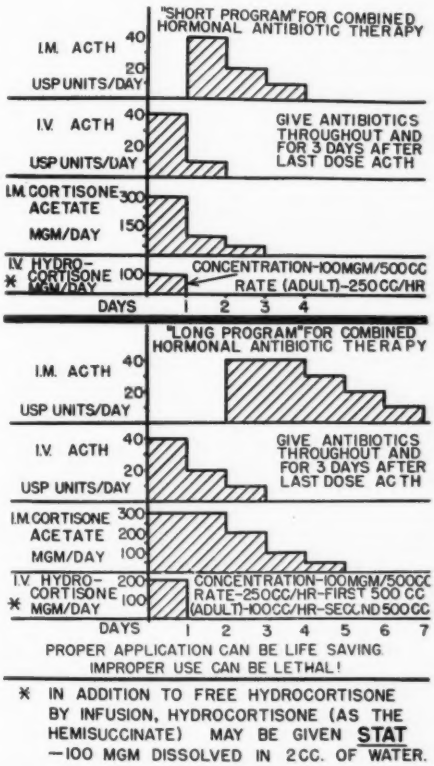

Fig. 2.—Program for corticoid treatment. Antibiotics are used simultaneously and continued for at least one week after cessation of the corticoid therapy.

Surgery is carried out as soon as the clinical condition warrants. The use of the short or

the long course of therapy is dependent on the severity of the illness. The short course is usually sufficient.

This report is based upon further experience with these agents over the past three years. Previous reports from this institution cover the other phases of our experiences.† This report covers a clinical summary of severely ill patients with peritonitis in the years 1952 through 1954. The patients were graded as to the degree of severity of their disease on the basis of I to IV, with Grade I and II being mildly ill patients with free fluid in the peritoneal cavity and a history suggestive of an acute abdomen, which is either due to traumatic perforation or inflammation of one of the intra-abdominal organs. The patients of Group III were more severely ill with elevated temperatures, elevated leucocyte levels, but no extreme toxicity. The Group IV patients were markedly toxic, often in shock, and moribund. The patients in this group are reviewed in detail. It is these severely ill patients who would be most benefited by this therapy.

A total of 50 patients in the severely ill group were found in the 233 patients with peritonitis in this institution. Of these 50 patients 19 did not receive the steroids—just the conventional therapy. Of the 19 only 3 survived, after a stormy postoperative convalescence. Of those who did not survive, five died before they could be restored to a condition in which operation could be carried out. One of those was a 63-year-old man who died while the incision was being made. He had been in shock, had a board-like abdomen, and a history of ulcer. It was found at autopsy that he had a perforated duodenal ulcer giving him peritonitis. In addition, another duodenal ulcer had penetrated into the pancreas causing a massive hemorrhage. The remainder of this group lived for varying time intervals after operation, succumbing to the various complications of their disease.

Thirty-one patients received the corticoid therapy; of this group twelve survived. In the group who did not survive, there were four patients who survived less than 24 hours after therapy was started. Two were newborn infants who had a perforated viscus diagnosed shortly after birth. Therapy, which consisted of combined hormonal-antibiotic treatment and surgery, was instituted immediately. They died within two and four hours following operation, respectively. It is felt that in these four patients there was insufficient time for any form of therapy to be effective.

† References 8-15.

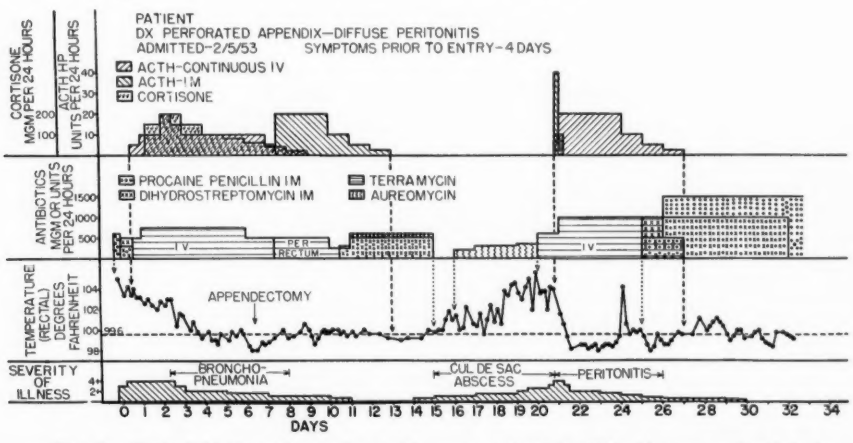

Fig. 3.—Clinical history of a patient with acute peritonitis. This history emphasized the need for prolonged antibiotic therapy and a second course of hormones in the face of complications.

Report of Cases

The following clinical summaries are illustrative of the type of patients treated and the results obtained.

CASE 1.—A girl aged 2½ years (Fig. 3) was admitted to the hospital with a history of abdominal pain, nausea, and vomiting which was progressive for four days prior to admission. She had the classical physical findings of a diffuse generalized peritonitis, and on admission her temperature was 104.8 F rectally. She was extremely toxic. She was placed on intramuscular procaine penicillin which was supplemented with dihydrostreptomycin. At the end of one day the temperature dropped to 103.8 F. Her extreme toxicity persisted; therefore, she was started on intravenous oxytetracycline (Terramycin) plus the program of corticoids. At this point the surgical consultants thought that it would be impossible to carry out any surgical procedure on this patient in that clinical state. On her third day of hospitalization, she developed symptoms of bronchopneumonia which were confirmed on x-ray. The corticoids and the intravenous antibiotics were continued. She gradually improved and on the seventh hospital day the patient was operated upon. At this time she appeared clinically well. The operative procedure was carried out because our earlier experiences indicated that the condition of these patients does not resolve spontaneously when they have a definite cause for the peritonitis. At operation a perforated appendix was found. She had generalized peritonitis. The appendix was removed. Her postoperative convalescence continued uneventfully until she was inadvertently taken off the antibiotics on the 16th hospital day. She again began to have an elevation of temperature. It was found on rectal examination that a cul-de-sac abscess was present. This was broken into during a digital examination on the 22nd day of hospitalization. She again developed clinical evidence of a generalized peritonitis. Treatment with the corticoids plus more vigorous antibiotic administration were reinstituted. The patient left the hospital clinically well on her 34th hospital day. This patient points out several features:

1. That the treatment of the surgical cause for the peritoneal contamination must always be carried out in spite of the clinical appearance of well-being in the patient.

2. That the antibiotics must be given for at least one week after conclusion of the steroid therapy.

3. It may be well to treat any severe complications in which there is a toxic response with another short course of the hormones.

CASE 2.—The next patient represents a child aged 8, who entered the hospital with a history of abdominal pain, nausea, vomiting, and fever for 15 hours. This patient had been treated 2 months previously in a private hospital for 25 days, with antibiotics, for what was diagnosed clinically as an

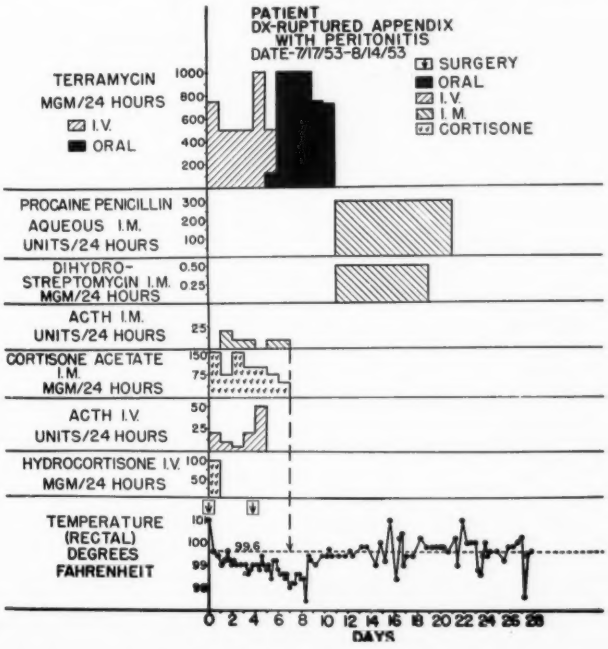

Fig. 4.—Clinical course of an 8-year-old boy with reperforation of an appendiceal abscess.

appendiceal abscess. On entry, this child was extremely toxic, although his rectal temperature was only 101 F on admission. A white blood cell count of 15,800 cells per cu. mm. with 24% immature polymorphonuclear leucocytes was found. The child was so ill that the surgical consultant advised nothing more than a drainage of the appendiceal abscess at this time. He was started on antibiotics and corticoids, as shown in Figure 4. At the end of 24 hours, he was afebrile and appeared clinically well. On the fourth day of hospitalization, the child was operated on and the appendix was removed. It was found that he had a reperforation of an acute purulent suppurative appendix. It was also found that although the peritoneal cavity contained a moderate amount of purulent material, the serosal surfaces were smooth and shiny and did not show any appreciable damage caused by the inflammation. He withstood the procedure well. The patient's postoperative course was relatively uneventful.

CASE 3.—A 3-year-old boy had a history of 28 hours with severe pain, vomiting, and on entry was extremely toxic (Fig. 5). On admission, his temperature was 105 F rectally. After repeated tepid baths his temperature came down to 101.8 F, rising to 104 F in spite of the fact that the patient was on intravenous oxytetracycline. The child was so severely toxic that no operation was carried out until he had been in the hospital for about 18 hours. He was started on the combined hormonal therapy two hours preoperatively. At operation an acute gangrenous appendicitis with perforation was found. The inflammatory reaction at the terminal ileum caused a small bowel obstruction. An appendectomy was carried out. His temperature fell rapidly after the operative intervention, but the patient remained clinically quite ill. On the third day of hospitalization, he was given 500 cc. of whole blood in addition to the antibiotics plus the combined hormonal therapy. On the 11th day, the drain which had been placed in the wound down to the peritoneum had begun to show an increased amount of drainage, and he developed a slight elevation in temperature. The drain was, therefore, removed on the 12th hospital day. The patient was dismissed from the hospital as well, on his 18th hospital day.

Not all of the patients treated in this fashion were of the pediatric age group. We have used this treatment in all age groups with the same indications. However, the two extremes in age present the greatest problem of marked reaction to infection.

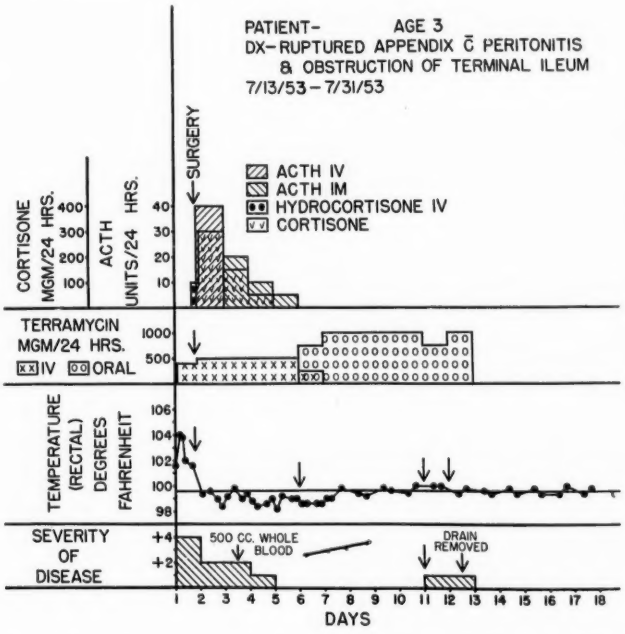

Fig. 5.—Combined corticoid-antibiotic and surgical therapy in a 3-year-old child.

CASE 4.—A man aged 60 entered the hospital in profound shock. His blood pressure was unobtainable on admission. He was unable to give a history. Physical examination revealed a silent, board-like abdomen. After inserting a plastic cannula into an arm vein and the administration of dextran plus

electrolyte solutions, the patient responded enough to give some history. His history was that he had severe abdominal pain for 24 hours prior to his admission. He had consulted a private physician several hours before entry; his physician gave him 15 mg. of morphine and sent him into the hospital. After the administration of the opiate, the patient went into profound shock at which stage he was seen at this hospital. After the administration of plasma expanders, his blood pressure rose gradually. At the time his history was taken, his blood pressure was 80/50 mm. mercury. It was not until the blood pressure had stabilized itself at 132/88 that the patient was considered a candidate for operation. This was four hours following his entry into our emergency room. Upon giving the patient an anesthetic, his blood pressure again dropped to an imperceptible level. The operation was delayed until a vasomotor response was obtained following the administration of phenylephrine hydrochloride (Neosynephrine), corticoids, and fluids (Fig. 6).

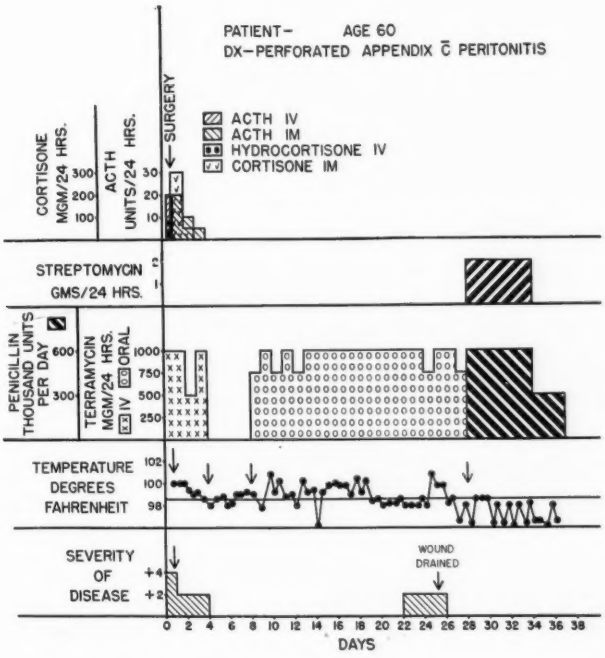

Fig. 6.—The clinical course of a patient aged 60 who entered the hospital in shock.

Exploration revealed a generalized peritonitis secondary to a perforated, gangrenous appendix. An appendectomy was carried out. The wound was closed without drains. The patient's convalescence was marred only by the formation of a wound abscess which was drained on the 25th hospital day.

Comment

The adrenocorticotropic and adrenocorticosteroid hormones are known to exert a marked anti-inflammatory effect. This effect is well documented.‡ In addition to the anti-inflammatory effect these hormones also seem to exert a toxin blocking effect.§ The mechanism for this effect is not well understood. However, on the basis of the experience of others in the treatment of extremely toxic persons with severe medical diseases, it was felt that this same effect might be produced in persons with severe fulminating peritonitis.|| It is in this group that these hormones have been used, in conjunction with chemotherapeutic and antibiotic treatment plus other supportive measures, in the past five years. Fortunately, there are too many patients of this variety even in a county hospital. In the

‡ References 1-4, 10, and 14.
§ References 3-9.
|| References 3-7.

series herein reported only 50 patients were so severely ill that they were considered candidates for this therapy. Of these, 19 did not receive the supplemental corticoid therapy for one or more reasons. Only 3 survived in contrast to 12 who survived of 31 patients on the corticoid therapy. In each group there were patients who were so severely ill that no form of therapy would be of benefit. These were not excluded from this study. Unfortunately, in a hospital dealing with indigents, the length of hospital stay cannot be used as a criterion for morbidity, since the length of hospital stay is determined by whether or not the patient has a home in which to convalesce, rather than the state of his health. No comparison was made in this regard. From the cases studied, we feel that where properly used the corticoids have permitted definitive surgery in patients who might otherwise not be operated on. It must be emphasized, however, that the adrenocorticotropin and adrenocorticosteroid hormones may mask the cause of the infectious process by reducing the toxicity and, therefore, one cannot use the clinical appearance of the patient as a measure of his true state. We, therefore, rigidly adhere to the rule that all patients who are treated with corticoids plus other measures for severe peritonitis *must* be treated surgically as soon as their clinical condition permits. We also found through bitter experience (Figs. 1 and 3) that the antibiotics must be continued for five to seven days following the conclusion of the corticoid therapy.

When properly used, therapy with the adrenocorticotropic and adrenocorticosteroid hormones in combination with antibiotics plus fluid and electrolyte replacement may lead to a better survival rate in patients who are seriously ill with peritonitis. These hormones permit one to carry out indicated surgical procedures in patients who would otherwise be too toxic to withstand the procedure.

Summary

A number of severely ill patients with peritonitis were treated with antibiotics in conjunction with adrenocorticotropin and adrenocortical steroid hormones, plus other supportive measures.

These hormones seemed effective in preparing patients who would otherwise be too severely ill to withstand operation. It must be reemphasized that definitive surgery should not be delayed because of the appearance of clinical improvement.

With the use of these hormones the antibiotics must be continued for at least one week following the termination of the hormone treatment.

An outline of the course of treatment is presented.

George Fukayama, Nancy White, and Maureen Donaldson, and her staff in the Medical Record Library gave valuable assistance in the publication of this work.

DISCUSSION

DR. ARTHUR J. HUNNICUTT, Oakland, Calif.: I should like to reemphasize some of the points that Dr. Henegar has given us so clearly.

These corticoids do not replace anything. By "anything" I mean they do not replace any of our usual therapy. These corticoids do enable the surgeon to borrow or to buy some time in which the surgeon can replace the electrolytes and get the patient in better condition.

To the degree that these corticoids block the manifestations of the disease, they also block one's clinical judgment. In these patients who are under corticoids you cannot rely on clinical findings to make up your mind as to the course of the disease. We feel this so strongly that we believe that the surgeon should commit himself in writing as to his definitive surgery and the time of his definitive surgery when the corticoids are started.

We have seen several disastrous instances in which the patient looked so well under the corticoids that the decision to operate was unduly postponed. Dr. Henegar illustrated this in the first case.

We have had some experience (about 15 cases in private practice) in using these corticoids in other surgical situations. These are more difficult to evaluate. We have used them in several instances in the preoperative preparation of patients who are undergoing surgery of large magnitude. We have used them in about five instances as an emergency procedure in the operating room. In

these cases it was our clinical opinion that these steroids were lifesaving or at least a definite aid in helping the patient to come through.

It is our opinion at the present time that probably, if there is an indication for these as an emergency procedure in surgery, the strongest indication is a falling blood pressure that seems to be out of proportion to the magnitude of the surgery and not accounted for by the blood lost.

We have used these in several instances in patients with severe postoperative complications, and in one or two instances our patients who had to be returned to surgery in their postoperative period. It seemed to help them over the hump, so to speak.

These corticoids are not always necessarily lifesaving. However, I do believe that we can say rather definitely from our experience that in no instance have we been sorry that we have used these steroids.

I was going to say that we have had no instance of failure of wound healing in the accumulated 100 cases in our Alameda County Hospital and in the private hospitals in Oakland. Dr. Henegar reminds me that we do have one, a patient with a closed loop bowel obstruction and in very poor nutritional status; so, how much of it to blame on the corticoids, we are not sure.

When I say we have had no instance of failure of wound healing, I am referring to the patients under these short-term corticoid therapies.

Finally, may I add a note of warning. There is not a universal awareness that, if a patient has been on long-term corticoids, he may have a partial or complete medical ablation of his adrenals. If such a patient undergoes surgery, his corticoid intake must be increased. His depressed adrenals without this support may be inadequate to meet this added stress of surgery.

DR. GEORGE C. HENEGAR, Oakland, Calif.: I simply want to say that I consider it a privilege to present a paper before this Association.

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EDITORIAL NOTE: The opinions expressed in this article, which was read at the 63d Annual Meeting of the Western Surgical Association, Seattle, Dec. 3, 1955, are a little at variance with general thoughts on the value of corticotropin and corticosteroids in infections. However, they might well be correct for the kind of cases and conditions under which they were employed and further experience may bear them out. In the meantime, caution should be used in the employment of corticotropin and corticosteroids in cases of peritonitis unless, as the authors have stated, operative treatment is planned and carried out just as soon as the patient's condition warrants.

Six Years' Experience with the Cleveland Cardiac Resuscitation Course

ROBERT M. HOSLER, M.D., F.A.C.S., Cleveland

After six years as associate director of Cleveland's * Course in Cardiac Resuscitation, I am obliged to repeat that cardiac arrest in the operating room is still an enigma and challenge to the surgeon and the anesthetist. Our experience has also led us to believe that the time has arrived when resuscitative procedures can and must be included in the treatment of the acute coronary problem. By that I mean that there are now a handful of cases on record which have been successfully revived even after suffering apparent death from acute coronary occlusion.

No doubt there are many similar persons who, if their hearts were given another chance, might function well for a considerable time in the future. They have good heart muscle except for a tiny area of slight damage. Yater [1] found, in his autopsy series of 950 men who died of coronary artery disease in the Armed Forces, that one-third showed no evidence of myocardial damage. Mechanism death occurred in well over 90% of all the victims of coronary artery disease. These hearts stopped because of a difference in electrical potentials resulting from oxygen differentials between the anoxic segment of myocardium and the normally oxygenated myocardium.

The future definitely holds some promise for those whom fate has been generous enough to grant a fatal "heart attack" in a location where trained personnel with the "know-how" and the proper equipment are available. Our conception of so-called death must necessarily undergo new consideration, for the death factor may at times be small and reversible. At this moment this statement will not be universally accepted, but will the future regard the following extraordinary incident commonplace.†

Recently in a Cleveland Hospital, a 65-year-old physician collapsed and for all intents and purposes died while walking out of a door near the hospital's emergency ward. This doctor had some time previously suffered a coronary occlusion, and only a few minutes before his collapse, an electrocardiogram had been taken.

Two surgeons were behind him, and they carried him to the nearby accident room, where adequate help and equipment were available. Without hesitation or delay, his shirt was ripped off and within two minutes his heart was being massaged and his lungs ventilated. The heart was in coarse fibrillation and after several shocks it was returned to a coordinated beat. He was successfully resuscitated with his shoes and trousers on. His postresuscitative course was uncomplicated except for a clouded sensorium for a few days and a slight wound infection. This was an outstanding example of clear thinking and courage. Previously another somewhat similar incident occurred in Philadelphia.

One feature apt to be overlooked is that this incidence dramatically and emphatically demonstrates that a small amount of oxygenated blood represents the difference between life and death in coronary insufficiency. Usually it is a problem of unequal distribution in the myocardium rather than

Received for publication May 4, 1956.

* Sponsored by the Cleveland Area Heart Society, 2073 E. 9 St.

† C. S. Beck, personal communication to the author.

in the amount available. In this instance, manipulation and surface excoriation effected this balance, so that six months later this man is in good health and has returned to the practice of medicine.

Until 1951 the pendulum of occurrence of cardiac arrest in the operating room was swinging alarmingly upward, but since that time through the unveiling and disbursal of old ‡ and new knowledge of the subject, the pendulum now appears to be on the downgrade. Why this queer lack of knowledge prevailed for 50 years in medical educational circles is difficult to explain. This subject from 1902 to 1950 seemed to be an underground tunnel, and then it suddenly emerged.

The average surgeon carries the thought that such a catastrophe "can never happen to me"; therefore he may neglect to apprise himself of methods to circumvent or combat this unexpected disaster. This is an entirely human reaction—just as when reading in the newspaper that a pedestrian has been struck down while crossing the street, one unconsciously says to himself "that will never happen to me." However, once it occurs, it may be too late in that particular instance, but humility will become the stepping stone to knowledge.

There is no need to frighten or allow patients to become frightened into believing that cardiac stoppage in the operating room is a common occurrence, but it is not a rarity. It will occur at least an half a dozen times each year in every good-sized hospital, which indicates its infrequency during the careers of many surgeons.

To point out further that the clinical phenomenon of cardiac arrest during an operation is not a rarity, the following figures of its incidence will subsequently be referred to.

There seems to be little agreement or comparison in the data accumulated by various authors. This is understandable, as there are so many variables and intangible factors that must be considered. Some authors appear to make an attempt to differentiate true primary cardiac arrest on the operating table from secondary arrest on the operating table. This is not a practical differentiation at the operating table, but only at the autopsy table. The practical result is to preserve the patient's life by immediate action. Let us not quibble.

It would appear that an average figure for general hospitals would indicate that cardiac arrest may occur once in every 2000 anesthetics, or slightly less frequently. It is also estimated that 10,000,000 surgical anesthetics are administered each year in the United States. If one were to use the round figure 1 in 2000, it might mean that there are 5000 tombstones dedicated to this clinical phenomenon each year. During the epidemic year of 1952, deaths attributable to poliomyelitis were between 3500 and 4000. This would suggest that it is a greater killer than dreaded poliomyelitis. Obviously not included in these figures are the anesthetics given by the dental profession. It has been determined that there are approximately 30,000,000 of this type each year.

In one large general hospital in Cleveland, 26,612 surgical anesthetics were given over a three-and-one-half-year period, there was an occurrence rate of 1 in 739, with a 33% survival rate. In one nearby 190-bed general hospital there occurred 18 sudden deaths on the operating table during a 17-month period, without a survival.

Certainly these statistics clearly denote that it is not a rarity. Another approach to this aspect of the subject may be taken by considering the number of surgical deaths in a general hospital, comparing the percentage cardiac arrest has played. For instance, in one 700-bed hospital § in 1952 there were 32 deaths on the surgical service, 5 of the 32 occurring from cardiac arrest. In other words, cardiac arrest as a surgical complication in this hospital accounted for 15½% of the deaths. Is it a rare surgical complication?

Fatalities in the operating room each year

‡ References 2-4.

§ Personal communication to the author.

from static electrical sparks are variously reported from 20 to less than 100. Compare the precautions, education, and available equipment that have been given and directed to combat these two unexpected and dissimilar operating room phenomena.

The best treatment for this condition is prevention. Planning for such an eventuality is one of the most successful ways to avert it. This planning must be on an individual plane as well as on an institutional plane. Hospital drill teams of the permanent staff (the white coat staff) should be organized. The knowledge, use, and whereabouts of special instruments and equipment should be learned. The house staff should have formal discussions and instructions on this important subject every six months; otherwise complacency will take over, and when the lightning strikes, the inertia which has been engendered cannot be quickly overcome. This is another way of saying that the persons in a position to carry out this procedure may have become "rusty." Delay or error in this instance can be the difference between life and death. Whenever death is imminent under anesthesia, there should be a means of alerting such a team. False alarms should be relished.

The closest collaboration must exist between the surgeon and anesthetist regarding the emotional and physical condition of the patient, the type of anesthetic, and the requirements of the operation. We are careful to avoid a multiplicity and overdosage of preanesthetic drugs; an adult is given 0.0006 gm. of atropine sulfate and a suitable sedative one-half hour before the operative procedure.

In some persons the specific cause of cardiac arrest is entirely clear and obvious. In many instances this is not the case; it may be the result of a chain of circumstances which are not well understood, or may have been ignored, and somewhere along this physiological chain a link is broken which precipitates the disaster. Many of the factors implicated do not seem important until after the catastrophe has occurred.

Almost without exception the cause of cardiac arrest ultimately resolves itself into a lack of oxygen in the vital tissues. Anoxia in this day and age constitutes one of the gravest hazards to the surgical patient, and the immediate effect on the brain and myocardium is the most serious. This lack of oxygen is the result of either impaired ventilation or impaired circulation, the former occurring more frequently. It is typical of severe anoxia that when respiration and circulation fail, they fail suddenly. Too often the incriminating expression has been used: "The patient was overdrugged and underoxygenated."

Briefly, the majority of the contributing causes may be found in the following categories: Position of patient, decreased vital capacity, tracheal obstruction, poor oxygenation, anemia, anxiety, insufficient atropine, shock, poor cardiac filling, torsion of the heart, excessive accumulation of carbon dioxide in spite of good oxygenation, vagal reflexes, errors of judgment, excessive numbers and quantities of preanesthetic and anesthetic drugs, individual idiosyncrasies, apathy, and cardiac disease.

The treatment of cardiac arrest has been confined to those persons who die in or near the operating room where equipment and a professional team are on hand. This procedure cannot be carried out alone, and the thorax cannot be entered without positive pressure apparatus. Anyone opening the chest on the golf course, and this has been recorded in the newspapers,‖ reveals his own ignorance of this subject.

In this discussion the steps for the treatment of this cataclysmic disaster will be referred to only briefly, as precise detailed instructions are found in other medical literature.[5]

In my opinion, the most important point in the resuscitation procedure is its separation into two distinct steps. Beck is responsible for this basic contribution. The components are 1. Part I. Reestablishment

‖ Cleveland, 1954.

of the oxygen system (the emergency act); 2. Part II. The restoration of the heartbeat. This separation makes it mandatory to assign proper importance to the various acts that are taken in the resuscitation procedure. The recognition that these are two separate and distinct steps has been frequently overlooked. This concept focuses attention on the oxygen system and not on the heartbeat. With a thorough understanding of this distinction, the problem of resuscitation becomes simple, provided one can place and keep first things first and can exert the necessary perseverance. The importance of each simple little step cannot be overemphasized, as failure in one may often account for failure to save a life. For instance, failure to make a large thoracotomy; movement of blood through massage would then be impossible. It would amount to tickling the heart.

What is meant by reestablishing the oxygen system? In simple understandable terms we mean performing three functions: First, get oxygen into the lungs. Second, have enough available hemoglobin to transport the oxygen. Finally, provide a dynamic pump to propel the oxygenated hemoglobin to the brain and other vital organs in order that they will remain viable. The "arrested heart" remains a satisfactory hydrodynamic pump, provided the surgeon gets his hand upon it and carries out manual massage. This act represents the crisis, and for successful resuscitation it must be established within three to four minutes, otherwise the brain will be irreversibly damaged. After the oxygen system has been started and kept in operation, the restoration of the heartbeat can be carried out without special reference to time. In the operating room the surgeon is confronted with two conditions of cardiac stoppage, namely, cardiac standstill and ventricular fibrillation. Fortunately, the former is encountered more frequently, as it is the easier of the two to treat.

The surgeon should not be in a hurry to close the chest as soon as the heart starts to beat. The heart should be carefully observed for a period of time; this time depends upon the individual surgeon's judgment. The patient should not be removed from the operating room until his color is good and his blood pressure and pulse are stable. Only then is it permissable to remove the patient to a recovery room and never directly to his room.

Drugs assume a minor role in the actual resuscitation act. If the oxygen system is reestablished with dispatch, there is little need for them. In the difficult case of restoring the heartbeat they are used as a last resort. Do not clutter up your mind or your operating table with drugs other than epinephrine and procaine, as their value has long been proved.

Certain equipment should be available in every operating room. Special equipment must be on the floor and always in working order. This applies as well for so-called minor operations as for major operations, regardless of the anesthetic employed. tions, regardless of the anesthetic employed. It would seem that the toll of cardiac arrest is exceptionally high in the presumably good-risk patient with a normal heart and lungs undergoing an elective procedure, while the patient whom we are reluctant to operate "sails through." Does this signify that in the former instance the surgical team was apathetic and not alert to the danger signals which may have been displayed?

The anesthetist should have a special kit consisting of a laryngoscope, various intratracheal tubes, connections, and lubricating jelly. A rubber bag, face mask, and 100% oxygen should be at the head of the operating room table.

An emergency sterile kit should be in the operating room at all times. It need not contain many instruments. It should include a scapel, a Finochietti or Bereford retractor, two sterile medicine glasses, two 10 cc. syringes, one with a metal tip, two ampules of 1% procaine, two ampules of 1:1000 epinephrine, two or three hemostats, surgical scissors, two electrodes, and a few sponges.

The above drugs are all that are necessary during the crisis. A tray of emergency drugs should be kept in the operating suite to be used by consultants or assistants. This tray is made up of ampules of atropine, lanatoside C (Cedilanid), caffeine, levarterenol (Levophed), mephentermine (Wyamine), quinidine, calcium chloride, and potassium chloride.

A foolproof shocking device or defibrillating machine is a necessity. In the strictest sense these machines do not comply with all the features of the fire code. However, the code permits the use of any equipment in order to save a life. There is no other practical method for restoring a coordinated beat to a human heart which has undergone ventricular fibrillation. Ventricular fibrillation is incompatible with life.

A Pacemaker is a valuable machine to have available during the postresuscitative period. Applied to a heart whose rhythm is slow and faltering, at times it can control and bolster the beat in a very effectual manner. It is my opinion that it should not be used during the emergency act, which I have previously defined. Others have great hopes that this machine when applied to the exterior of the body will act as a self-starter for the arrested heart. My experience with laboratory dogs led me to believe that the desired results will not occur when cardiac stoppage has taken place for any ordinary length of time within the normal time limitation of three to four minutes. Applied to a dilated and cyanotic heart it has no effect. Under clinical circumstances, the greatest opportunity for success in resuscitation arises from first reestablishing the oxygen system. This is the emergency act.

In the long and difficult resuscitative procedure, a breathing machine is a definite benefit and not a luxury. A rubber bag filled with oxygen can be squeezed by hand, and the lungs can be made to inflate and deflate by this method. However, over a long period of time a respirator will undoubtedly do a much better job than can be done by hand. The machine does not tire out and lose efficiency.

An electrocardiograph should be available in surgery. However, it is of no value unless a competent cardiologist is readily available to interpret the record. Furthermore electrical impulses may be recorded as complexes four to six minutes after visible cessation of the heartbeat.¶ Emphasis should be placed upon the fact that unless it has been previously attached, it has no place in the emergency act. However, it has a distinct place in the postresuscitative and postoperative period.

The question is often asked: "Who should carry out a resuscitation procedure and when should the procedure be undertaken?" Any doctor capable of undertaking any surgical operation should be capable of properly carrying through a resuscitation procedure, at least the emergency act. Once the oxygen system has been established, consultation can be summoned. In fact, a complete understanding of the subject should be a requirement. Society has a right to demand of a surgeon, the anesthetist, and the institution in such a catastrophe that they make an intelligent effort at resuscitation. Success resulting from the application of the procedure cannot be required of them.

This procedure should rapidly be placed into motion on all patients being operated upon if there is a disappearance of the pulse and blood pressure, regardless of age, known heart impairment, or known poor risk. Taking too long to confirm the fact of a breakdown of the oxygen system will only jeopardize the patient's chances of survival. The oxygen system must be reestablished as soon as possible. Every second must count. If the surgeon is in a position to palpate a large artery, very little time will be wasted in confirmation. Thereupon, the left thorax should be widely opened immeditaely to expose the heart. It is now agreed that under such circumstances exposure of the heart is a diagnostic procedure.

¶ Reference 5, page 103, Figure 7. Reference 6.

Successful resuscitative procedures have been caried out on many patients who previous to their operation had suffered from coronary occlusions and infarcts. This knowledge should not deter the surgeon from going ahead with an earnest attempt. I know of two cases in which the finger has been stuck through a paper-thin myocardial infarct.# At this point, the outlook would seem futile, yet these patients were successfully revived.

At no time during the immediate postresuscitative interim should the patient be moved directly from the operating room to his room. If his condition permits, it may be possible to move him to a recovery room adjacent to the surgery. The patient will need constant immediate attention, necessitating possibly more than one nurse for an indefinite period.

It is extremely important to be absolutely certain of an adequate airway at all times during the immediate postoperative interval. Postoperative suction of the airways must be observed frequently in all patients. The intratracheal tube should not be removed until it is ascertained that the patient will take over satisfactorily breathing on his own. The respiratory function can be mechanically controlled for several hours with an endotracheal tube in place. A tracheotomy set must be available.

The patient should be kept in a flat or slightly Trendelenburg position until reaction is complete. It has been found that after the intracheal tube is removed, respirations may be less labored if one shoulder is elevated by placing a pillow beneath it, thus turning the patient slightly to one side. This position is also beneficial in case of regurgitation. The unoperated side should always be up and free. Nasal oxygen is administered after spontaneous respirations have resumed.

The blood pressure, pulse, and respiratory rate should be recorded every five minutes for the first few hours. At times the blood pressure ebbs away in spite of the use of intravenous fluids and vasopressors. Fluids must be given judiciously, and one's choice of these fluids and of all medications must depend a great deal upon the patient's response. Blood is recognized as the fluid without a rival for its excellence in the treatment of existent circulatory disturbances, especially for the replacement of blood volume. If blood is not immediately available, blood substitutes (plasma, dextran) will have to suffice temporarily for replacement of volume. The circulatory system at this juncture will not tolerate overloading.

It is prudent to administer the following in the postresuscitation period (providing that they had not already been given): After standstill, atropine sulfate grains 1/150, intravenously. In most cases a half a digitalization dose of lanatoside C intravenously. After ventricular fibrillation, an intravenous solution of 20% dextrose and 3% saline for a short period. This tends to counteract an increase of the postassium ion in the blood stream. The increase of this ion in the blood stream has been found associated with the hypercapnial [7] state following ventricular fibrillation and with serious arrhythmias recorded by the electrocardiogram.

Cardiac disturbances must usually be diagnosed with the aid of an electrocardiogram and a consultant. This is especially true in the evaluation of disorders of rhythm. Supraventricular arrhythmias are usually innocuous.

The patient's temperature is to be taken every hour for the first eight hours. A rapid rise in temperature usually indicates cerebral damage. An oxygen tent may serve a twofold purpose, that of supplying additional oxygen and also that of a cooling medium. The ordinary cooling practices of ice bags and alcohol rubs are to be employed.

Acute cerebral edema is usually the cause of death in those persons whose circulatory systems have been restored to normalcy. This may occur 10 to 12 hours or several

Reference 5, page 160.

days later. In those cases in which there is a question as to whether the period of cerebral anoxia was longer than three minutes, it is advised[8] that 25% human serum albumin be administered intravenously in 100 cc. amounts every three hours as often as it appears necessary. The usual methods to promote dehydration are carried out. Workers[9] in other fields have under similar instances of edematous tissues suggested the use of corticotropin (ACTH), 120 mg. each day. The rationale being without complete destruction, under such circumstances corticotropin may suppress the inflammation and thereby reduce the swelling and pressure, which in turn would lead to better circulation in the brain. Convulsions, if they should occur, are controlled by intravenous sedatives.

Stephenson reports that about 13% of cardiac arrests occur in parts of the hospital other than the operating room. A goodly share of these take place in the recovery room. Most of these are due to anoxia occurring in the recovery room or an accumulation of carbon dioxide during the operation. In the latter case a situation is set up in the recovery room whereby serious arrhythmias occur, the blood potassium is at its highest level,* the heart is extremely irritable, the adrenals are stimulated to generate an overdose of epinephrine, and the nurse in attendance may suddenly be confronted with ventricular fibrillation.

A careful record of the total intake and output for 24-hour periods is routinely tabulated. Routine laboratory as well as special laboratory procedures may be necessary as problems present themselves. Particularly one must be alert for a lower nephron syndrome resulting from renal anoxia.

Certain drugs which are known to be helpful are kept in a tray labeled "emergency tray" in the recovery room and operating room.

A survey of our course in cardiac resuscitation was carried out late in 1954. Questionaires were sent to approximately 500. Total replies numbered 276, which is good considering there was no return envelope nor postage. The summarized results are as follows:

	Yes	No	Unanswered
1. Have you had occasion to use resuscitation procedures since taking this course?	85	191	
2. If so, were you successful?	44	36	6
3. Do you find that knowledge in this subject has helped prevent possible disaster?	235	19	22
4. Please report interesting cases, etc.			
5. Does your hospital have an organized program for the prevention and management of cardiac arrest?	206	52	18

To date over 1000 have participated in this course, which started as an orphan. Geographically they have come from 34 different states in the U. S. A. Foreign countries include Canada, Phillipines, Brazil, Spain, England, Switzerland, Puerto Rico, Cuba, Guatemala, Belgium, Ecuador, Mexico, Scotland, Argentina, Formosa, Japan, and France.

The recipients of university degrees from numerous schools in 29 separate foreign countries are included in the participation group.

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Conservative Surgical Treatment of Peptic Stenosis of the Esophagus

Report of a Case Complicated by Perforation

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Although peptic stenoses of the esophagus frequently respond to peroral dilatation, those which cannot be so dilated, or are complicated by severe bleeding or perforation, often require surgery in the form of plastic procedures or some type of gastric or esophageal resection. The subject has been comprehensively reviewed by Benedict and Gillespie [1] and Benedict.[2]

The following case is presented because it represents a successful result of a surgical approach which has not been stressed.

A 40-year-old white man was readmitted to the Ray Brook State Tuberculosis Hospital for the fifth time on Jan. 30, 1954, with severe dysphagia, weight loss, and pulmonary tuberculosis. He had experienced essentially no gastrointestinal difficulty until Oct. 18, 1950, when he developed epigastric distress followed by lower abdominal pain. On Oct. 20 an appendiceal abscess was drained. On the first postoperative day the patient's abdomen became distended and he vomited several times. A gastric tube was passed, and continuous suction was employed for three days. After removal of the tube, the patient experienced intermittent dysphagia, retching, and substernal and epigastric discomfort. Fluoroscopy on April 30, 1951, revealed intermittent obstruction at the lower end of the esophagus, apparently the result of spasm. On May 29, 1951, because of exacerbation of appendicitis, an appendectomy was performed. After surgery, nasogastric suction was employed for about one week because of distention and vomiting. After removal of the gastric tube, dysphagia gradually increased in severity and frequency, in spite of prescription of antispasmodics and dietary measures. Roentgenographic examination in June, 1952, revealed an esophageal stricture (Fig. 1). Because of increasing dysphagia, the patient consulted a surgeon who performed esophagoscopy. It was noted that esophagitis with ulceration and stricture was present. During an attempted dilatation of the stricture, the esophagus was perforated. Thoracotomy and suture of the perforation were performed on the same day (Dec. 3, 1952). The immediate postoperative course was uneventful. However, about two weeks after the thoracotomy, the patient developed fever and infiltration in his right lower lung field as seen on roentgenogram. This cleared with antibiotic therapy. Dysphagia gradually progressed until, at the time of his fifth admission to Ray Brook State Tuberculosis Hospital, the patient could barely swallow liquids. Previous admissions to Ray Brook State Tuberculosis Hospital were as follows: Oct. 22, 1942, to June 7, 1945; Nov. 16, 1946, to June 19, 1947; May 18, 1950, to June 15, 1952; Jan. 3, 1953, to March 8, 1953. A two-stage seven-rib right

Fig. 1.—Stricture of the esophagus.

Submitted for publication Feb. 29, 1956.

From Ray Brook State Tuberculosis Hospital.

thoracoplasty was performed in October and November, 1951. Following the thoracoplasty, there had been no evidence of activity of the patient's tuberculosis.

Results of Physical Examination.—Physical examination revealed the following relevant findings: temperature, 99.8 F; pulse, 116; respirations, 16; blood pressure, 130/82. The patient appeared chronically ill and had obviously lost a great deal of weight. There was evidence of a right seven-rib thoracoplasty, and there were well-healed abdominal and bilateral thoracotomy scars. Fine rales were heard over the apex of the right lung posteriorly and over the upper third of the left chest anteriorly.

Laboratory Studies.—Sputum was negative on smear and culture for Mycobacterium tuberculosis. Blood count and results of urinalysis were within normal limits. Roentgenogram of the chest revealed scattered nodular disease in both pulmonary apices, with no evidence of recent change when compared with previous films. Gastric analysis on Dec. 12, 1954, was as follows:

	Free HCl, Degrees	Total Acid Degrees
Fasting	24	52
One-half hour after 50 cc. of 7% alcohol	46	63
One hour after 50 cc. of 7% alcohol	34	56

Course in Hospital.—About two weeks after admission, the patient developed an elevated temperature to 101.6 F associated with substernal discomfort. He was given a swallow of a small amount of thin barium, and it was seen to enter the posterior mediastinum to the right of the midline. On Feb. 24, 1954, a posterior mediastinotomy followed by a jejunostomy was performed. The abscess gradually healed except for a small sinus connected with the esophagus above the stenosis, which was now almost complete. On iejunostomy feedings the patient gained weight. On Sept. 30, 1954, esophagoscopy was performed, and through the esophagoscope an unsuccessful attempt was made to guide a fine Jackson bougie through the stricture. It was noted that the mucosa in the narrowed region was very red and bled easily. On Dec. 3, 1954, the patient was taken to the operating room, where a left thoracotomy was performed. The basilar portion of the left lung was freed and the interior mediastinum exposed. The lower esophagus was surrounded by scar. It was obvious after some dissection that it would be exceedingly difficult to free the esophagus. It was, therefore, decided to dilate the esophagus in retrograde manner. Accordingly, a radial incision was made in the diaphragm, preserving the continuity of the rim of the esophageal hiatus. No abnormality was noted in the upper abdomen except for the enterostomy. There was no hiatus hernia. A 1-in. incision was made into the stomach near the cardia. Jackson bougies from 9 F. through 30 F. were inserted into the lower esophagus and carefully guided through the stricture, which was located at approximately the junction of the lower and middle thirds of the organ. The length of the stricture was approximately 1 to 2 cm. in its narrowest portion. A small gastric tube was then threaded cephalad through the stricture, having been tied to the tip of a bougie which had been passed by the oral route. The opening in the stomach was then repaired with an inner Connell suture of 00 Atraumatic chromic absorbable surgical (gut) suture and a seromuscular layer of interrupted Lembert sutures of 0000 nonabsorbable surgical (silk) sutures. The diaphragm was repaired with interrupted 00 nonabsorbable surgical (silk) sutures. The chest was closed with catheter drainage. Postoperatively, the patient's course was uncomplicated. On Dec. 23, the gastric tube was removed and the patient was allowed an increasing diet by mouth. On Jan. 7, 1955, esophagoscopy revealed persistent mucosal redness without ulceration in the stenotic area.

Fig. 2.—Spot roentgenogram of the esophagus taken with the patient swallowing thin barium while in about a 45-degree Trendelenburg position.

Dilatation to a 32 F. bougie was accomplished with ease. Progressively larger dilators were employed at weekly intervals, until on March 7 a 50 F. bougie was passed. At first Jackson bougies were employed endoscopically; later, Hurst mercury-weighted bougies were substituted. Dilata-

tions were continued at increasingly longer intervals. When the esophagus was last examined endoscopically on Dec. 21, 1955, it appeared normal except for a slight hyperemia near the cardia. The 9-mm. Jackson esophagoscope encountered no obstruction, even though the last dilatation had been performed more than three months previously. Roentgenographic examination on Dec. 15 revealed an essentially normally functioning esophagus without evidence of stricture (Fig. 2). The patient could swallow normally while in about a 45-degree Trendelenburg position. There was no evidence of regurgitation of barium from the stomach into the esophagus. Symptomatically, the patient gradually improved until about March, 1956, when he was taking solid food without difficulty. He rapidly regained weight. Although he has not followed a bland dietary regimen or taken other precautions usually prescribed in the medical treatment of esophagitis, he has not been troubled by belching, eructation, or pyrosis. His tuberculosis remains inactive.

Comment

Since resection or plastic surgery of the lower esophagus is often followed by the occurrence of esophagitis, many attempts have been made to avoid these procedures or to discover functionally satisfactory substitutes.* Although this patient presented at least two indications for resection or plastic surgery (perforation and stricture which could not be dilated endoscopically or with the aid of a swallowed string), it was possible to treat him successfully by performing retrograde dilatation of the exposed esophagus. In spite of the extensive inflammation in and about the organ, a good anatomical and functional result was obtained. Although a single instance does not have widespread implications, it would seem that this method of therapy might be worthy of trial in other selected cases.

This patient is interesting for other reasons. He developed esophagitis following the use of a gastric tube, a sequence which has been reported by others.[1] This occured in the absence of symptoms of gastric hyperacidity or hiatus hernia. There is every evidence that the intrinsic and extrinsic sphincter mechanisms were functioning effectively, since regurgitation did not occur when the patient was placed in the Trendelenburg position. Yet, once esophagitis appeared, it tended to prepetuate itself until dilatations were effected. This evidence tempts one to speculate that perhaps the esophagitis, originally the result of vomiting and regurgitation about a gastric tube which interfered with the competence of the sphincter mechanism of the organ, was perpetuated by the retching and regurgitation which ocurred whenever food became lodged in the narrowed lumen, and that once the obstruction was completely relieved the cause of regurgitation and consequent esophagitis ceased.

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Summary

A case of severe peptic stenosis of the esophagus, complicated by perforation and impossible to dilate endoscopically, was successfully treated by retrograde dilatation of the exposed organ.

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Coexisting Diverticulitis and Carcinoma of the Colon

Comprehensive Study on Survival

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The physician is faced with distinguishing between diverticulitis and carcinoma all too frequently in the management of colonic disease. With the advent of intestinal antibiotics, Wangensteen suction, and proper understanding of electrolytes and blood volume, a more aggressive surgical approach to diverticulitis has been made. However, due to technical difficulties accompanying resection of colon involved with active inflammation, definitive surgery is often long delayed to allow regression of the inflammatory process. If carcinoma is later discovered alone or accompanying diverticulitis, the mistake may well have deprived the surgeon of the opportunity of total excision of the malignant process.

Diverticulitis accompanying carcinoma of the colon has long been considered an unusual combination. With the steadily increasing number of elderly persons and the recognized increased frequency of diverticulitis in older age groups, patients experiencing the disease simultaneously should likewise be seen more frequently.

The purpose of this article is to determine whether the prognosis in patients with carcinoma of the colon is lessened by the coexistence of diverticulitis and, if so, to clarify the factors responsible for the difference in survival. Only patients demonstrating, both grossly and microscopically, the presence of both diverticulitis and carcinoma of the colon were used in this study. This series was made possible through the interest and cooperation of many physicians well recognized for their knowledge of diverticulitis and carcinoma, from whom by personal communication * the data on 112 cases with the coexisting diseases were obtained. Six patients were added by me to provide a series of 118 persons.

Submitted for publication March 20, 1956.

From the Department of Surgery, Ohio State University College of Medicine.

Age and Sex

The youngest and oldest in the series were both men, 43 and 91 years of age, respectively. The average age was 64 years, with the peak incidence during the 56- to 65-year decade. Of the total series, 57% were men. The proportion of men affected was essentially the same as in published reports on carcinoma of the colon and rectum,† but the average age and the age of peak incidence for patients with coexisting diseases were approximately 10 years greater.‡

Sites of Coexisting Lesions

The sites of both lesions in each patient were noted. Both lesions were in the same segment of colon in 73%. Carcinoma developed distal to the diverticulitis in 17%, with the malignancy proximal to the diverticulitis in the remaining 10%.

The possibility of carcinoma influencing development of inflammation in diverticula

* Contributors to this Series were Drs. Charles W. Mayo, Thomas A. Shallows, John J. Morton, Claude E. Welch, Robert F. Rauch, Joseph Shaiken, Carrington Williams Jr., Robert M. Moore, Henry K. Ransom, Harvey B. Stone, Kirby A. Martin, William A. Johns, Robert J. Rowe, Vincent W. Archer, and R. Russell Best.

† References 1, 3, and 4.

‡ References 3 and 5.

lying adjacent or proximal was considered, though it could not be proved. In all probability diverticulitis arising distally has no direct relationship. The rapidity of metastatic spread of carcinoma occurring in the same segment as diverticulitis may be influenced by the increased regional vascularity created through inflammation.

Prognosis

Entire Series.—Table 1 lists the follow-up course of the 118 patients. Five or more years following resection, 24% were alive and free of carcinoma, with an additional 5% living and well up to five years. Fifty-one per cent were dying or had died of recurrent carcinoma. Only 3% were lost to follow-up. The over-all operative mortality of both palliative and potentially curative procedures was 12%. Comparison of survival rates for carcinoma of the colon and rectum among published reports is exceedingly difficult due to variations in standards of analysis. However, the 24% five-year survivals suggest a significantly poorer prognosis than that reported § for cancer of the colon and rectum alone. The 12% operative mortality likewise is considerably higher than that reported by most authors for carcinoma of the colon and rectum.

TABLE 1.—*Follow-up Course of Entire Series*

	No. of Patients
Alive and well, 5 yr.	28
Alive and well, 3 to 5 yr.	3
Alive and well, 1 to 3 yr.	3
Dead or dying of recurrent carcinoma	60
Noncarcinoma deaths	6
Operative deaths	14
Lost to follow-up	4
	118

Ninety-one patients (77%) were considered to have received potentially curative resections, while 27 persons (23%) had palliative resections, colostomies, or explorations.

In 56% of the 118 patients, carcinoma extended beyond the confines of the bowel wall.

§ References 1 and 6.

Potentially Curable Cases.—Of the 118 persons, 91 received potentially curative resections. In 52% of these patients there was no demonstrable carcinoma beyond the confines of the bowel wall. The other 48% had either lymph node or direct invasion of surrounding structures. Table 2 lists the follow-up evaluation of the 91 patients with potentially curative resections. Excluding operative deaths and patients lost to follow-up, 35% of the 91 patients were alive and well five or more years following resection, with an additional 8% alive and well from one to five years. Of those with potentially curative resections, 50% have to date died of recurrent carcinoma. In analysis of carcinoma of the colon by Grinnell [3] and Gilchrist,[2] using similar criteria for evaluation of "curable cases," 53% and 66% respectively were alive and well five years following resection, while 38% and 30% had died of recurrent carcinoma. These comparisons indicate a distinctly poorer, but by no means hopeless, prognosis for patients with combined carcinoma and diverticulitis.

TABLE 2.—*Follow-up Course of Potentially Curable Patients*

	No. of Patients
Alive and well, 5 yr.	28
Alive and well, 1 to 5 yr.	6
Dead of recurrent carcinoma	40
Non carcinoma deaths	6
Operative deaths	7
Lost to follow-up	4
	91

In order to determine the effects of lymph node and direct invasion on prognosis, patients with and without carcinoma spread at operation were evaluated separately.

Of the patients without malignant spread at the time of resection, and excluding operative deaths and patients lost to follow-up, 57% were alive and well five or more years following resection, with only 21% having died of recurrent carcinoma.

These findings were similar to those in

studies of others || on prognosis of carcinoma of the colon and rectum alone.

Of patients receiving potentially curative resections with carcinoma spread at surgery, 11% were noted to be alive five years after resection, while 79% had died of recurrent carcinoma.

When the reported five-year survival rate of 26% to 42% for comparable lymph-node-positive series of carcinomas of the rectum and colon is considered,|| the gravity of encountering lymph-node-positive cases with the coexisting diseases can be easily understood.

Presence of an Inflammatory Mass

An appreciable inflammatory mass was noted in 66% of the entire series, with 27% showing minimal degrees of inflammatory reaction. Insufficient data hindered accurate determination of the presence or absence of inflammation in 7%. The influence of an inflammatory mass on prognosis was felt to be worthy of investigation not only because of increased vascular flow accompanying inflammation but also because of the added technical difficulties associated with removal of such lesions.

Seventy-eight patients were recorded as having an inflammatory mass present. Of these, 21 received palliative and 57 potentially curative procedures. Of the curative resection group, 28% were alive and well five years or more following resection. Forty-seven per cent died of recurrent carcinoma. The operative mortality for resections in patients with an inflammatory mass was 12%.

Thirty-two patients had only a minimal inflammatory mass. Five received palliative and 27 potentially curative resections. Of the curative resection group, 37% were alive and well five years or more following surgery, with an additional 19% well from one to five years. Thirty-three per cent have died of recurrent carcinoma. There were no operative deaths in this group.

The impression gained from the above data is that an inflammatory mass appears to have an adverse effect on prognosis from both increased metastatic spread and increased operative mortality.

Error in Preoperative Diagnosis

Why a case of coexisting carcinoma and diverticulitis should be diagnosed and managed preoperatively as diverticulitis is not difficult to understand. Delay in the surgical removal of carcinoma, particularly when associated with regional increase in vascular supply, may well mean, however, the difference in ultimate survival.

For 110 patients, data were sufficient to determine whether a preoperative error in diagnosis had been made. Error in diagnosis had occurred in 36 instances, while 74 cases carried the proper diagnosis.

Of those with an error in diagnosis, only 17% were alive and free of carcinoma five or more years after resection. Sixty-one per cent had died of recurrent carcinoma.

In contrast, of the persons with the correct preoperative diagnosis, 30% were well five or more years after resection. In 45% recurrent carcinoma developed and they died. The operative mortality of both groups was essentially the same.

The impression drawn from the above data is that an error in preoperative diagnosis decreases moderately the chance of survival by providing further time for the spread of the malignant process. The risk of surgical intervention, however, is not altered.

Previous Episodes of Diverticulitis

If carcinoma arises in a patient experiencing recurrent bouts of diverticulitis, symptoms related to malignancy may go unrecognized. The frequency of malignant spread away from the bowel wall in patients with and without previous episodes of diverticulitis was tabulated in an attempt to determine whether patients having previously known diverticulitis should expect a poorer chance of survival with the development of a malignant lesion. Adequate infor-

|| References 2, 3, and 6.

mation regarding previous episodes of diverticulitis was present for 84 patients, of whom 46 had experienced such bouts of the disease, while 38 had never been affected.

Of the previously afflicted patients, 15% were well and free of disease five or more years after resection, with an additional 9% well at intervals from one to five years. Fifty-seven per cent had already died of recurrent carcinoma. Of the patients free of prior inflammatory disease, 32% were alive and well five or more years after surgery, with an additional 3% well one to five years. Forty-five per cent had died of recurrent carcinoma.

No significant difference in carcinoma metastases between the series with and that without previous episodes of diverticulitis was noted, for cancer spread beyond the bowel lumen was recorded for 46% of the series with previous episodes of diverticulitis and for 53% of the group without prior inflammation. From the above data the chance for survival appeared to be minimally, if at all, diminished for patients having previous episodes of diverticulitis.

Duration of Symptoms Prior to Resection and Its Effect of Survival

The average duration of symptoms of those receiving potentially curative resections was found to be nine months, with a median of six months. The average duration of symptoms in patients given palliative surgery was 10 months, with a median of 6 months.

Patients undergoing either palliative or potentially curative procedures, for whom an error in diagnosis preoperatively had been made, noted symptoms averaging 12 months, with a median of 10 months, while those with accurate diagnosis prior to surgery averaged 5 months, with also a median of 5 months.

From the above data it may be concluded that factors other than duration of symptoms are apparently responsible for determining extent of spread. The data, however, substantiate a commonly accepted fact —an error in preoperative diagnosis promotes further tardiness on the part of both the patient and the physician in achieving proper surgical management of the malignant process.

Persons receiving potentially curative resections were classified into four groups, depending on duration of symptoms prior to resection, and evaluated for percentage of malignant spread beyond the bowel wall and rate of survival. The tabulation separated patients with symptoms lasting 0 to 3 months, 4 to 6 months, 7 to 9 months, and over 10 months.

By far the lowest incidence of malignant spread and highest five-year survival rate were achieved in patients receiving surgical treatment within three months of the onset of symptoms. The frequency of malignant spread and percentage of patients living five years or more varied insignificantly in groups with symptoms present more than three months.

Comment

Both diverticulitis and carcinoma of the colon occur most frequently in elder age groups. Patients presenting altered bowel habits, melena, lower abdominal mass, or left lower quadrant pain, therefore, must be investigated for both diseases. If sigmoidoscopic examination reveals no abnormality, the diagnosis of colon pathology and distinction between the two diseases usually rest with interpretation of the barium-enema x-ray examination. In many persons the roentgenologic findings are equivocal. Patients having carcinoma and not diverticulitis or having the coexisting diseases may be denied the opportunity for cure if the physician considers the lesion purely inflammatory. Likewise, previous episodes of diverticulitis in a patient may provide reason for complacency of the physician, and symptoms derived from a more recent carcinoma of the colon may be overlooked.

It would be improper to urge colon resection for diverticulitis purely on the basis of possible coexisting carcinoma, but it is surprising that a more aggressive surgical ap-

proach has been so slow to develop for patients demonstrating stenosis, massive hemorrhage, perforations, and fistula formation with their relatively high morbidity and mortality.

With good intestinal antibiotics, knowledge of the value of fecal stream deviation, and present-day understanding of both blood volume and fluid and electrolyte balance, recurring diverticulitis or initial diverticulitis in persons of the relatively young age group, even without its serious complications, should be considered more frequently a surgical disease, particularly since medical therapy is fraught so often with recurrent episodes of inflammation in the permanently damaged bowel.

One of the gravest situations to arise in a patient with diverticulitis is the development of a coexisting carcinoma. The extreme seriousness and adverse effect of diverticulitis on prognosis for cancer patients have at least in part been shown. The fundamental reason for poor survival rates is similar to that shown for carcinoma alone—the presence of malignant spread beyond the confines of the intestinal wall at surgery. The percentage of long-term survivors with coexisting diseases is considerably less than with carcinoma alone. The reasons undoubtedly are multiple. The presence of inflammation with increased blood supply enhances dissemination of the malignant process and hinders proper execution of adequate surgery. Moreover, the occasional failure to recognize coexisting carcinoma, even at surgery, leads to a somewhat less than adequate removal of the lymphatic drainage area.

If improvement in prognosis for persons with both diseases is to be had, a more aggressive approach toward questionable lesions must be formulated. However, as in all fields of medicine, the results derived from prevention by far exceed those from attempts to cure. Resection of colon involved with diverticulitis, though perhaps not lessening the incidence of carcinoma, rids the patient of a segment of chronically diseased bowel and at the same time eliminates one of the most frequent sites of malignant change.

Summary

An evaluation of prognosis of 118 persons with coexisting diverticulitis and carcinoma of the colon is reported. A significantly poorer prognosis is noted among patients with both diseases than among those with carcinoma alone.

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Axillary Node Examination in Breast Cancer

Clearing and Sectioning Technique in Search of Metastasis

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Prognostication for the patient undergoing radical mastectomy for carcinoma is based primarily on involvement of the axillary lymph nodes removed at time of dissection. The practical importance of this method need only be mentioned here, for most surgeons realize that when cancer of the breast is still limited to the breast itself the chances of being permanently cured of that lesion are decidedly better than if there is even minimal spread to axillary nodes.

The converse is also true; i. e., the patient whose operative specimen shows metastatic axillary involvement, particularly if several nodes are involved, has far poorer chance of permanent cure. Whether the primary lesion is really limited to the breast is difficult, if not impossible, to prove; however, the converse provides us with a relatively easy, rapid, inexpensive, and dependable method of judging the patient's course.

Although Monroe [4] was able to relate better five-year results to a greater number of lymph nodes found in the operative specimen (which indicated to him a more thorough dissection of the axilla) rather than just to metastatic involvement of the nodes, most of us depend for our prognosis upon the actual microscopic proof of metastatic spread to these nodes.

As indicated above, the true value of pathological examination of axillary contents in determining prognosis depends on both the extent and thoroughness of the axillary dissection by the surgeon and on the interest and thoroughness of the search for lymph nodes by the pathologist. There can be little question also that the actual position of involved nodes in the axilla may have as much, or more, prognostic value as the number of nodes involved.

The methods used in examination of the specimen vary with each laboratory, and the results obtained likewise vary. We began questioning our own methods when in 1948 Saphir and Ambromin [6] reported that 10 of 30 cases studied showed involvement of axillary nodes only on serial sectioning, after routine sectioning had shown them free of metastases. As pointed out by others (Ackerman [1]), Saphir's routine examination disclosed an average of only five nodes per case, and these are the nodes also serial-sectioned. The reason for the small number removed at radical mastectomy, found at routine examination, or studied microscopically, is not obvious; at any rate, we were sufficiently disturbed by this report to institute the following study. No effort here will be made to correlate the clinical with the pathological findings or to explore prognosis as such.

Recorded for publication June 11, 1956.

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Methods

The study was divided into two parts: (1) a project of clearing the entire axillary contents to obtain lymph nodes missed on routine examination and (2) serial-sectioning of all nodes from all cases which after routine examination and clearing (if necessary) still failed to reveal metastasis.

(1) In this study, the axillary contents were routinely searched for lymph nodes, which were then sectioned and examined microscopically (one section per node). Only one of the many surgeons performing these operations ever tagged the axillary contents to indicate level of tissue; thus the entire axillary mass was treated as a whole, though, if unwieldy, the contents of some cases were divided into smaller segments to facilitate the clearing. The entire contents were then subjected to a clearing technique consisting essentially of fixation by formalin, dehydration in increasing concentrations of ethyl alcohol, and clearing, with the use of either methyl salicylate or cedar wood oil. After clearing (in usually 24 to 48 hours) the specimen was again examined for nodes which might have been missed in the routine examination. These nodes, many of which were as small as 1 to 2 mm. in diameter, were then sectioned and examined (one section per node). Comparison of the two groups was then made.

(2) In each case, the above-mentioned sectioned nodes which were found not to show metastasis were sectioned serially in a further search. This is an enormous task, and, even as an experimental study, we rapidly realized the impracticability of producing for study each section cut from the node. Therefore, the nodes were sectioned at 4μ thickness and every third section was studied. It is felt that this procedure is adequate, since sectioning every 12μ should section any neoplastic cell, which is many times the size of a normal erythrocyte (about 7μ). A variant of this method was undertaken by making sections at 10μ thickness and studying every section.

All these sections were then studied as before.

Results

As shown in Table 1, a total of 37 cases were found to have negative axillary lymph nodes on routine examination and single sectioning, averaging 5.4 nodes per case. The cleared specimen then revealed an additional 12.8 nodes per case (average), making a total of 18.2 nodes per case found and examined by single section. In only 1 case out of the 37 were metastases demonstrated. There was involvement (Figs. 1 and 2) in two of the three additional nodes found by clearing the axillary contents. This case gave us an error in diagnosis of 2.7% of the cases studied.

In another series of specimens, whose data are not presented here, we cleared and sectioned the nodes even though metastatic involvement had already been proved by routine examination. These statistics clearly show that almost always the axilla containing metastatically involved lymph nodes contains also a much larger number of lymph nodes as found on routine examination than the axilla not showing metastatic involvement (averaging 11.0 nodes per positive case versus 5.4 nodes per negative case). However, this ratio is almost reversed by clearing the specimen and combining the two groups; viz., average of 12.0 nodes per positive case versus 18.2 nodes per negative case. This may be easily explained by the presence of the reticuloendothelial hyperplasia seen accompanying the metastatically involved nodes, rendering them easier to find on routine examination.

The above-described case of error of our

TABLE 1.—*Results in Cases with Negative Nodes on Routine Examination*

	Values
Number of cases in which nodes were negative on routine examination	37
Number of nodes found and examined in routine manner	199 (av. 5.4/case)
Number of nodes found on clearing specimen	473 (av. 12.8/case)
Average number of nodes found on combined technique	18.2/case
Number of positive nodes found on clearing	2
Number of cases in which positive nodes were found on clearing	1
Per cent of error in routine versus clearing technique	2.7%
Per cent of error in routine versus clearing technique	0.3% nodes

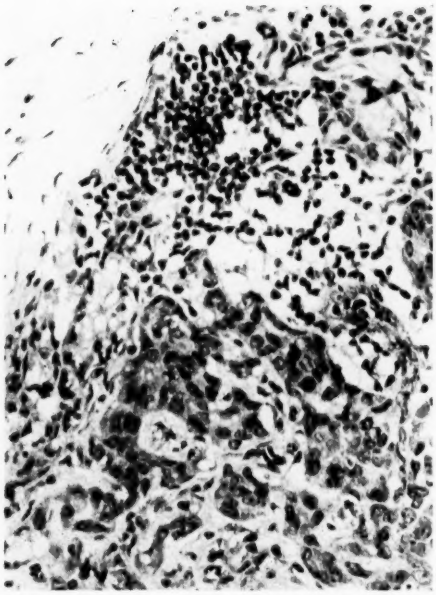
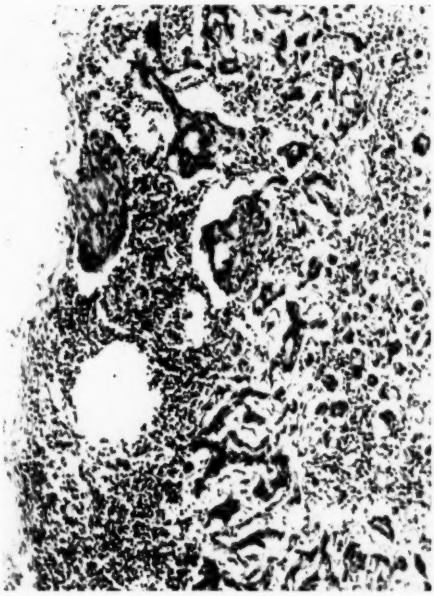


Fig. 1 (Case 7).—Single sectioning of this node, which was found on clearing the specimen, showed complete replacement by tumor. Reduced from mag. × 400.



2. Fig. 2 (Case 7).—One of the other two nodes found on clearing was extensively infiltrated by metastatic carcinoma. Reduced from mag. × 200.

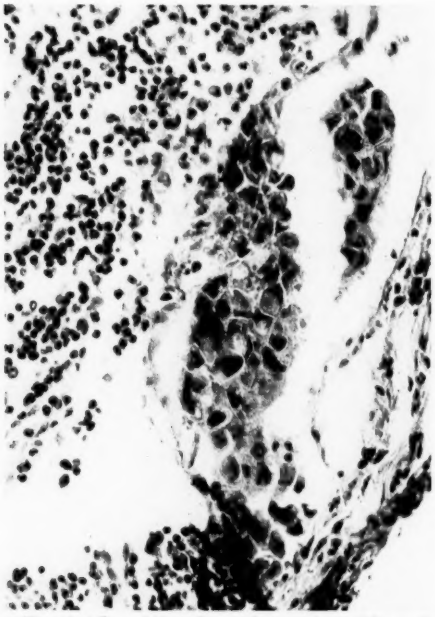


Fig. 3 (Case 16).—On serial sections this peripheral sinus involvement was found in three sections only. Reduced from mag. × 400.

Fig. 4 (Case 26).—One of three nodes found on clearing the specimen which showed this type of peripheral sinus involvement in serial sections. Reduced from mag. × 800.

TABLE 2.—*Results of Serial Sectioning of 646 Nodes*

	Values
Number of cases in which nodes were negative on routine examination and clearing	35
Number of nodes sectioned serially	646
Number of nodes found positive on serial sectioning but negative on single sections in routine examination and clearing	4
Number of cases in which positive nodes were found on serial sections but not on single sections	2
Per cent of error determined on serial sections	5.7% cases
Per cent of error determined on serial sections	0.6% nodes
Combined per cent of error of routine examination versus clearing plus serial sections	8.1% cases

routine examination was one of the few exceptions to these findings. In this case only six nodes were found on routine examination, and single sections of each were negative for metastasis. Yet only three additional nodes were found when the specimen was cleared, and two of these three were almost replaced by tumor.

Serial sectioning of the 646 nodes (Table 2), revealed only 4 to be involved by tumor. All four showed only peripheral sinus involvement by minute clusters of cells (Figs. 3 and 4). Three of these involved nodes were found in one case, five nodes having been found on routine examination and twenty-one nodes when the specimen was cleared. The three nodes positive on serial sections were found on clearing the specimen.

The other case in which involvement of 1 node was found on serial sections produced only 2 nodes on routine examination and 13 nodes on clearing. The node shown to be involved (Fig. 3) on serial sections was one of the two nodes found on routine examination.

In summary, of the cases studied so extensively, clearing the specimen and single sectioning the nodes changed the prognosis in only one case; serial sectioning of all negative nodes changed the prognosis in only two cases, and this was possible only because the additional nodes were found on clearing in one case. In all, the ratio of error was 8.1% of cases when the two additive methods were combined, only 5.7% of cases for serial sectioning all negative nodes, and 2.9% of cases on serial sectioning of the routinely-found nodes.

Comment

Several workers have reported on the relative value of clearing the specimen in search for lymph nodes. Pickren [5] cleared 75 cases and compared the results with 75 cases of routine examination; he found 65% increase in the number of nodes by clearing but only 27% increase in positive nodes. He found no significant difference in the number of cases found positive in the two groups. Of most importance, however, is the fact that he obtained no error (in cases) by routine examination.

Davis and Neis [2] cleared 77 consecutive cases and found an average of 31.4 nodes per case with variations from 10 to 73 nodes. Hood and Fleming [3] cleared 16 cases, found 5 positive cases, 2 of which it was felt would have been overlooked on routine examination because of the very small size of the nodes. In 1948 Monroe [4] had cleared 87 cases and taken multiple sections of each node (2 to 10 sections per node) to arrive at the conclusion alluded to above.

We are of the definite opinion that the time and expense necessary for clearing studies on mastectomy specimens are not commensurate with the results obtained. Likewise, serial sectioning is far beyond the practical limits of the surgical pathology laboratory, even of large university medical centers, considering the benefit derived for the patient or physician.

Summary and Conclusions

Of 37 axillary specimens subjected to a clearing technique, search for lymph nodes, and single sectioning of these nodes, the prognosis was changed in only 1 case.

Of 35 cases in which all nodes seen on single sections not to be involved by metastatic breast cancer were sectioned serially, only 2 cases had their prognosis changed, and in 1 of these serial sectioning of the nodes found on routine search without clearing would have proved sufficient.

Each of these additional methods of studying lymph nodes is found too time-consuming and otherwise expensive to be of value as a routine method. Indications are that the best practical method of determining axillary metastasis consists of a very careful initial search for nodes, employing, if necessary, a strong background light and perhaps making three or more sections from each node found.

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Resistant Trichomoniasis in the Female

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Every physician who treats women is plagued with cases of resistant and recurrent trichomoniasis. The factors responsible for the resistance to therapy and the recurrences after successful treatments are not always clear. Perhaps if we could find the few missing links in the etiology and the life cyle of the Trichomonas, our understanding would be more complete. My colleagues and I believe that trichomoniasis is commoner in women than in men and that the infection is frequently transmitted by sexual intercourse. The disease may be asymptomatic, and both men and women can be carriers. Exacerbations could be precipitated in part by a change in the accompanying bacterial flora.

Of the vaginal discharges in women, 50% harbor Trichomonas vaginalis. Recent reports on nonspecific male infections harboring Trichomonas reveal incidences of 12% to 15% (Durel and associates, Allison, Feo, and others). At times, the Trichomonas organisms are difficult to find and can easily be overlooked, particularly in the male, when wet smears of the urethral and prostatic secretions are not routinely utilized. In other words, the actual incidence of male trichomoniasis may be greater than is now ordinarily believed or recognized.

The object in presenting this paper is to report our treatment experiences in 40 cases of vaginal and urinary trichomoniasis in which the urinary tract appeared to be the primary resistant focus. The common involvement of the urinary tract has been known and previously reported by Allen, Sar-Louis, Hesseltine, Rodecurt, Manwell, Rakoff, Schneider, and others. Allen and Heckel studied 43 women cystoscopically and noted that the inflammatory changes were limited to the vesical neck and urethra.

Trichomonas organisms have been recovered from many orificial organs of the body, including the vagina, uterus, tubes, Bartholin's and Skene's glands, urethra, bladder, prostate, kidneys, mouth, and intestine. Bernstine and Rakoff recognized Trichomonas organisms in the urinary tract as secondary invaders in one-third of their cases, and their treatments included urethral instillations. Sar-Louis suggested urethral treatments with a blower and magnesium trisilicate parasitical powder. He regarded the urethra as a focus and found that eradication of this focus prevented recurrences.

In August, 1955, Kean stated that trichomoniasis may be primary in the urethra but that the dual involvement was imperfectly understood. He found vaginal trichomoniasis and Escherichia coli cystitis frequent companions and suggested that the bacteria rode up the urethra on the backs of the Trichomonas organisms.

Our understanding of this dual involvement in women is based on our experiences in observing trichomoniasis in men. My observations on the male date back to 1929, when I reported the first two cases on record of Trichomonas prostatovesiculitis. We have found a damaged and strictured male urethra extremely vulnerable to Trichomonas (12%). The cases we are now reporting revealed chronic urethral foci with lowered local resistance to infection and Trichomonas invasion. The eradication of these urethral foci has resulted in the clearing of the urinary and vaginal trichomoniasis.

Submitted for publication Feb. 16, 1956.

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Read at the Meeting of the Chicago Gynecological Society, Chicago, Dec. 16, 1955.

Summary of Cases

We have been privileged to see 43 patients with chronic urinary and vaginal trichomoniasis, of whom only 40 were treated, 2 in the office and 38 in the hospital with office follow-up. The infestation in the two office-treated patients failed to clear after one year's treatment. One did not return for hospitalization, and the other had a hysterectomy and failed to return. Of the 40 patients, all were white, 22 were married, 13 were single, and 5 were divorced, widowed, or separated. Twenty of these women had been pregnant, bearing 26 children, and 6 had had abortions. Twenty (50%) were menstruating, while 20 were menopausal (18 by hysterectomy). The youngest patient was 19 years of age, the oldest 76, with an average age of 40 years.

Symptoms.—The duration of symptoms varied from 1 to 18 years, with an average of 4.8 years. Among symptoms pertaining to the urinary tract, 22 women had frequency, 20 burning, 15 urgency, and 18 nocturia. Nine of the 40 women gave a history of gross hematuria. Vaginally, 14 women complained of itching; 37 had a discharge, while 3 had none. Three patients gave a history of Trichomonas vaginitis. Motile Trichomonas organisms were found in the 37 women with a vaginal discharge. Six patients complained of incontinence (four incontinence or stress and strain and two of the urgency type).

Physical and Urine Examinations.—Examination of the abdomen revealed no abnormalities in 32 women. There was localized or diffuse tenderness in eight. Palpation of the urethra revealed thickening in 30, tenderness in 6, discharge in 1, and visible caruncles in 3. Skene's ducts were found thickened in 35 urethras, while 5 seemed normal. Stripping of the distal urethra and Skene's ducts in 35 examinations revealed motile Trichomonas organisms in 19 (54%). The voided urine specimens revealed that 27 patients had no red cells, 9 had 0-10, 2 had 10-20, and 2 had 100 or more per high-power field. Twenty-four specimens had 0-10+ cells, 10 had 10-20 cells, 1 had 40-50, while only 4 had many pus cells per high-power field. Motile Trichomonas organisms were found in the urines of the 40 patients (32 in the hospital and 40 in the office). Two patients had residual urine (one 500 cc. and the other 200 cc.). Thirty-nine urine specimens were cultured, and 11 showed a single organism infection, while 13 showed a mixed infection. Fifteen urine cultures (37%) revealed no growth. A breakdown of the positive cultures showed that the Micrococcus pyogenes var. albus was found in 14 specimens, E. coli in 10, streptococci in 5, Aerobacter aerogenes in 3, Proteus in 2, and Alcaligenes in 1.

Cystoscopy-Urethroscopy. — Thirty-eight patients were subjected to cystourethroscopy in the hospital under caudal block and intravenous thiopental sodium (Pentothal sodium) anesthesia. The McCarthy panendoscope or resectoscope was used for the examinations and treatments. Fourteen patients had precystoscopic intravenous pyelograms. Five patients had hydronephrosis, requiring surgical correction in two and ureteral dilatation in three. Two patients had a solitary kidney. Eight cystograms revealed bladder hypertrophy, four with residual urine.

Cystoscopy showed a normal bladder mucosa in 37 patients; mild hyperemia occurred in 14 of these. One nonspecific bladder ulcer was recorded. The bladder wall seemed hypertrophied in nine patients; the bladder neck was inflamed in two and fibrosed in nine. Hyperemia of the trigone was noted 27 times; in 11 cases the trigone was covered with an irregular whitish membrane. The trigone was thickened and elevated in three cases. The urethral lesions noted in 38 patients were granulations (soft and hard) in 27, mucosal cysts in 10, polyps in 4, sclerosis in 4, hyperemia in 1, and contracted external meatus in 4, while 2 patients had normal urethras.

Treatments.—Forty patients had had previous vaginal treatments. Eleven had had

urethral therapy consisting of instillations, dilatations, and antibiotics. In half (50%) of these patients the symptoms persisted, and the other were plagued with recurrences.

Our treatments consisted of removing all urinary foci which could possibly serve as primary Trichomonas foci. After preliminary excretory pyelograms, combined urethrocystoscopic examination and treatments were routinely carried out. The treatments consisted of 19 urethral fulgurations (including fulguration of the trigone in 11), 11 urethral fulgurations with transurethral removal of deep urethral and vesical neck tissues, and transurethral resection only in 8. In 34 patients Skene's ducts were catheterized with an illuminated speculum and a blunt probe. Electrosurgical incision into the lumen of the urethra destroyed these ducts as a focus of infection. In 11 urethras, one or more supernumerary ducts were found; one patient had seven. A meatotomy incision was made when the meatus was small or contracted. Meatal polyps and caruncles were removed. All caruncle tissue was biopsied. After the operation, a 22 F. or 24 F. Malecot or Foley catheter was left in situ for 48 to 72 hours.

Postoperative Care. — Dihydrostreptomycin and penicillin were given intramuscularly twice daily while the catheter was in place. Oral medication was substituted on the third and fourth days. Sensitivity tests were used to aid in selecting the drug of choice. To the nervous woman, oral phenobarbital was given morning and evening. After the removal of the catheter, patients were made ambulatory and allowed to take sitz baths once or twice daily. Some patients had little postoperative discomfort, while in others the dysuria was intermittently severe. It took approximately four to six weeks for the urethra to heal. The healing was expedited by the use of antibiotics. After the healing was complete and the urine was clear, the urethra was calibrated and dilated once or twice if necessary. Previously prescribed vaginal treatments were resumed at home and continued while the urethra was under observation and treatment.

Postoperative Complications.—The treatment complications have been few and were not troublesome. The disadvantages are four to six days of hospitalization and four to six weeks' postoperative morbidity. Patients with stress and strain incontinence can be made slightly worse because of loss of the urethral spasm. Temporary postoperative incontinence which lasted from 4 to 12 weeks was noted in three patients. One patient developed a soft urethral stricture in the resected area which yielded to dilatation. One patient had gross bleeding from an incised Skene's duct, but hemorrhage was easily controlled by a pressure dressing and an ice pack. Late bladder hemorrhage has not occurred, but it could easily happen. The possible need for readmission is another disadvantage of our treatment regimen, usually resulting from incomplete eradication of all urethral foci. Five patients were admitted twice for treatment, while three others were admitted three times. In other words, eight patients (21%) required two or more hospital admissions and treatments to obtain a negative result. Our records show that the eight re-treated patients remained well, except for one who had a temporary recurrence after one year. Further studies indicate that seven of the eight patients with readmissions had anomalous supernumerary paraurethral ducts. In our opinion, anomalous ducts predispose to persistent trichomoniasis. The detection and destruction of all these anomalous ducts is by far the most difficult treatment problem to overcome in this group of patients.

Results

Our results have been surprisingly good. In the follow-up period the Trichomonas organisms seem to disappear after 30 to 90 days, along with the pus and red cells in the urine. Thirty-two of 40 patients (80%) seemingly were cleared of urinary and vaginal trichomoniasis. Four (10%) cleared

patients had temporary recurrences after one to two years. They were cleared again after a short course of urinary and vaginal re-treatments. Two failures were noted after one year's office treatment. These patients should have received hospital treatment. Six (15%) hospital patients had insufficient office follow-up to record the end-results, although two (5%) appeared to have been cleared. To our knowledge, there was no patient who was made permanently worse following the above urethral treatments. All these patients except four have been treated since January, 1948. Extended post-treatment follow-up in the majority of patients has been in the hands of the referring physician. More recurrences may have taken place which have not been brought to our attention.

Pathology

We have the microscopic tissue sections from 11 patients who were operated upon.

Resected bladder neck tissue, showing nonspecific subacute and chronic inflammation, with grouped lymphocytic infiltration and preglandular squamous epithelium; reduced about 2/5 from mag. × 220.

They all show evidence of chronic infection (Figure). Seven tissue sections show definite evidence of vesical neck fibrosis; three show muscular hypertrophy and fibrosis, and in one there were tissue changes compatible with a diagnosis of chronic cystitis. In no instance have we been able to demonstrate the Trichomonas organisms in the tissue sections. Our laboratory technician, Miss Mary McNichols, at one time showed me a large group of Trichomonas organisms (150 or more) expressed from a Skene's duct. We interpreted this finding as evidence of a Skene's gland Trichomonas focus.

Comment

Our observations concerning these 40 patients are not conclusive, but they strongly suggest that such resistant and recurrent cases may harbor a primary urinary and urethral focus. Other investigators (Karnaky, Reich and associates, Shelanski and Savitz, Brady and Reid, Hartwell, and others) have noted urethral, urinary, and vaginal involvement, but no definite urinary therapy has been recommended. Included in the present series are three cases previously reported in 1948 which strongly suggested the urethra or Skene or Bartholin gland involvement as the primary Trichomonas focus.

Many factors of human trichomoniasis remain obscure. Both men and women are afflicted with Trichomonas. Sexual intercourse is one common avenue for dissemination of the organisms. Sexual relations may well account for the recurrences after treatment. Previous studies do not favor rectal or oral contamination as etiological factors. The infection is probably more widespread in men than is now believed, and this could be one major factor in female dissemination. Observations in the male show that a devitalized strictured urethra is susceptible to Trichomonas vaginalis. Our studies in the female suggest that chronic female urethritis and skeneitis have low tissue resistance to infection and Trichomonas invasion. The large percentage of negative urinary cul-

tures found in this series would indicate that the Trichomonas is not a bacterial carrier but rather a secondary invader after the soil has been prepared by chronic infection and lowered tissue resistance. This view is supported also by the fact that, when the infected urethral foci are destroyed, the new tissues are better able to resist infections and recurrent Trichomonas invasion. Eradicating all existing urethral foci will clear urinary and vaginal trichomoniasis, provided there are no coexisting vaginal foci. All chronic vaginal foci, such as cervicitis or Bartholinitis, should be removed by surgical treatment. In our experience such combined treatments offer these chronically ill patients more permanent relief than any treatments which have been previously suggested. To my knowledge, there is no oral or local medication that will permanently clear these patients of resistant trichomoniasis.

Summary and Conclusions

Forty patients with urinary and vaginal trichomoniasis are reported on. Thirty-eight were treated by urethral surgery and two in the office. Surgical treatment of the urethral foci resulted in clearing the resistant and recurrent trichomoniasis in 32 (80%) patients. Eradication of all urethral and vaginal foci is necessary for the permanent clearance of resistant female trichomoniasis.

Anomalies of the distal urethra are common. Surgical removal of all anomalous paraurethral ducts is technically a difficult procedure. In seven of our eight patients with readmissions to the hospital, additional anomalous ducts were found and their treatment resulted in clearing of the trichomoniasis.

Through normal sexual intercourse, the Trichomonas organisms are frequently transferred from the male to the female or vice versa.

Addendum

In their recent article (*Obst. & Gynec.* 7:128-136 [Feb.] 1956), Perl and associates reported their experiences in the treatment of male and female trichomoniasis with oral Tritheon (2-acetylamino - 5 - nitrothiazole), 100 mg., t. i. d., p. c., for 10 days. They were able to clear 49% of their 188 patients, as shown by negative cultures and wet smears for Trichomonas vaginalis. They urge similar treatment for all men whose wives have trichomoniasis.

In view of the above report, resistant trichomoniasis may be treated first with oral Tritheon and the failures considered for surgical treatment as outlined in the manuscript.

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A Simple Apparatus for Rapid Serial Roentgenography

Design, Construction, and Operation

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and
LAURENCE MISCALL, M.D., Jamaica, N. Y.

During the past decade, angiocardiography has been a widely employed diagnostic technique, owing largely to the efforts of Robb and Steinberg [5] and Dotter and Steinberg.[2] The importance of contrast visualization has been well established, and certainly it is more widely desired by radiologists, cardiologists, internists, and surgeons particularly. Experience has shown that such studies are most informative when multiple serial roentgenograms are made at very short intervals during the passage of the contrast medium through the heart and great vessels. Although cineroentgenography ultimately may become the method of choice in such examinations, at present not only is the detail inferior to that of direct roentgenography but also the cost of the equipment is high and its use rather technical. The trend has been toward rapid serial roentgenographic exposures with the use of either roll film or lightweight cassettes. Such equipment insures a comprehensive visualization. Although units of this type and some of the more expensive biplane design are now commercially available, there is a need for less expensive and less intricate apparatus. These are particularly useful in centers where a large number of studies are done, or in a smaller institution where the fewer studies do not merit great expenditure.

This report details the construction of a simple, efficient, safe cassette changer which permits the exposure of serial films (11 in. $\times$14 in.), faster than one per second.[2] Material and methods in angiocardiography and pulmonary angiocardiography are given.

Construction of Apparatus

Although many mechanically simple and practical devices for obtaining rapid roentgenograms have been described,* most of the reports have dealt with their operation rather than with the details of construction. The construction and operation of this device are simple. It has been more than satisfactory in serial angiocardiography in a large series of cases at the Triboro Hospital. No claim is made for originality in principles of design and operation. To the somewhat similar apparatus described by McGregor [3] in 1949, some useful features have been added. The complete details of construction and operation permit the acquisition of an extremely efficient unit at low cost. With this apparatus, one can obtain serial timed exposure of 16 films (11 in.$\times$14 in.) in about 10 seconds.

The materials needed for construction are detailed in the Table, and with the aid of Figures 1 and 2 these can be assembled readily. Since some allowances must be made for the small variations in the sizes of cassettes and x-ray tables, the following order of assembly is suggested.

Submitted for publication March 24, 1956.

From the Surgical Service, Triboro Hospital for Thoracic Disease, Jamaica, N. Y. Director of Surgery, Triboro Hospital (Dr. Miscall).

* References 1, 3, 4, 6-9.

1. Assemble Parts 2 and Part 1.

2. Assemble Parts 3, 4, and 6 and attach to Part 11.

3. Attach Part 12 to Part 11.

4. Assemble Parts 1, 19, 18, and 14, place these in Part 15, and attach Part 15 to Part 12. (Note Figure 2 for position of Part 15.)

5. The distance between Parts 15 and 17 is equal to the width of the x-ray table (Fig. 1).

6. Attach Part 17.

7. Attach Part 16.

Parts List

Part No.	Length, In.	Width, In.	Thickness, In.	Quantity	Comment
1	34	15	¾	1	Plywood
2	14¾	2	½	2	Wood
3	17½	9	½	1	Wood
4	12½	9	½	2	Wood
5	17½	13½	½	1	Lead-covered wood or lead plywood
6	17½	9	½	1	Lead-covered wood or lead plywood; bevel lower-inner edge
7	17½	12⅛	½	1	Lead-covered or lead plywood
8	17½	12⅛	¼	1	Bakelite
9	17½	24¼	½	1	Lead-covered or lead plywood
10	15½	5	1	1	Wood
11	81¾	1	1	2	Wood
12	64⅝	17½	½	1	Wood
13	12⅛	1	¼	2	Wood
14	12	3	¾	1	Wood
15	17½	2	2	1	Wood
16	28	2	¾	2	Wood, length should equal width of x-ray table
17	17½	6	2	1	Wood
18	79	2	½	2	Wood
19	15	3	¾	1	Wood
20	15⅛	12⅛	½	1	Not shown; to be attached to under surface of Part 5
21	15	12	5/16	2 or 3	Not shown; to be used as dummy cassettes

1. Parts 1, 18, and 19 are bolted together.
2. Parts 14 and 18 are bolted together, and bolt head is countersunk into Parts 18.
3. Although Bakelite is desirable for Part 8, it is not essential since Parts 8, 13, 7, and 9 may be replaced by one piece of plywood measuring 48½ in. × 17½ in. × ½ in. The second 12⅛ in. from the magazine must not be covered with lead.
4. Surfaces which come into contact with each other—Part 12 with Part 19 and Part 14 and 15—may be lined with felt.
5. The inner surface of Part 10 which comes into contact with the cassette may be lined with felt.
6. You will notice in Figure 3 a block of wood has been placed securely on Part 1. This will assist in stopping the forceful forward thrust of Part 1. This wood is lined with felt or foam rubber where it strikes Part 3.

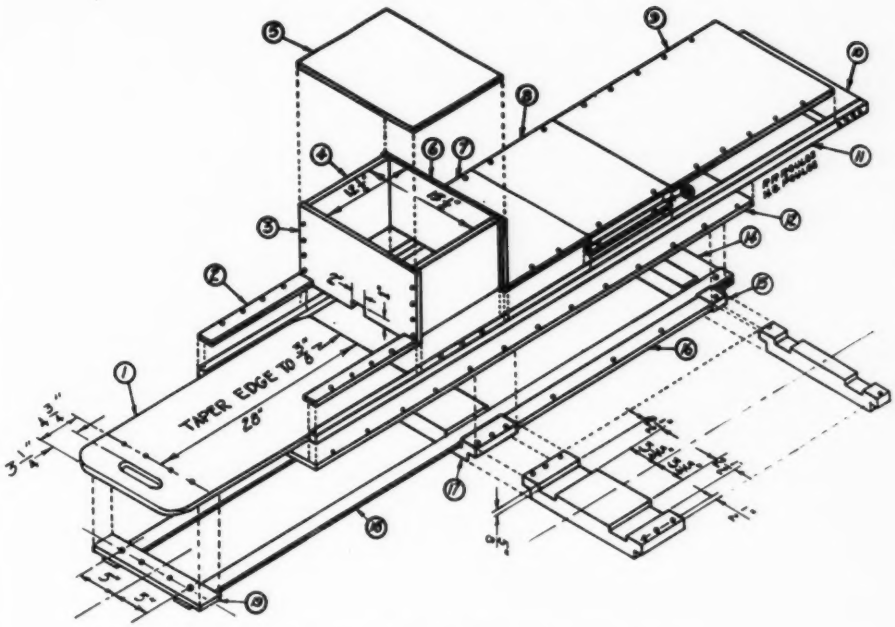

Fig. 1.—Detailed plan of construction; for individual parts, see text.

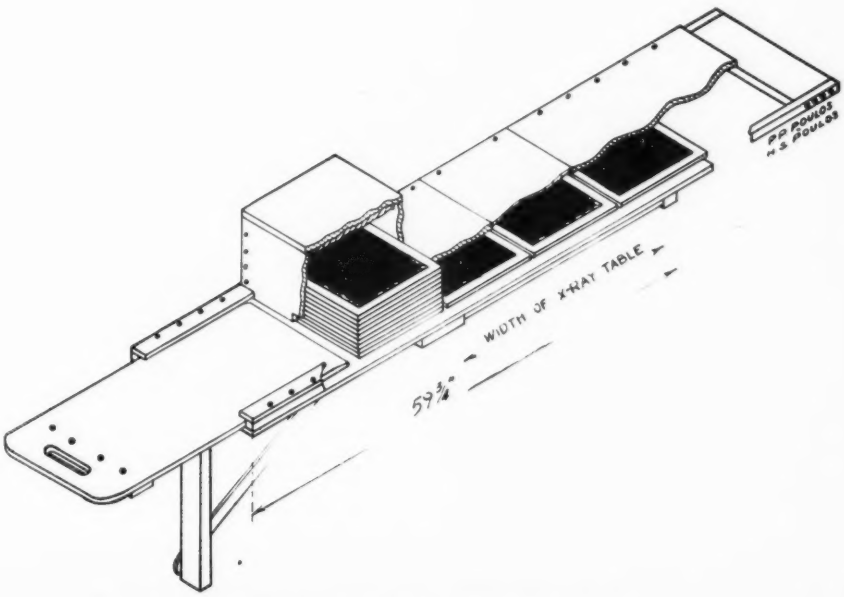

Fig. 2.—Graphic illustration of loaded magazine ready for use.

At this point attach Part 10 to Part 11. Now load the magazine with at least four cassettes and run them through the apparatus. If necessary, adjust Part 10 so that the cassette drops down freely on withdrawal of the injection handle.

8. Attach Part 10 permanently.

9. Finally, attach Parts 7, 13, 8, and 9 (see Note 3, bottom of Table).

The small window in Part 3 permits emptying the tunnel of its plates by using a long, thin piece of wood. The top one-third of Part 3 may be removed so that the magazine can be loaded during operation to expose an unlimited number of plates.

10. Figure 3 shows a patient in position for injection. Lead shields are easily adapted and should be used for protection, especially if a large number of procedures are completed.

Operation of Apparatus

The operation of the apparatus is relatively simple (Fig. 3). The apparatus is readied for use by loading the magazine with a dummy cassette on the bottom and top and slowly delivering one dummy and two unexposed filled cassettes into the tunnel. Up to 16 loaded cassettes are placed in the magazine. The backward motion of the handle is limited by Part 14 contacting Part 15. During the forward motion of the handle, the bottom plate of the magazine is moved the distance of one cassette into the tunnel. The handle is fully withdrawn, and the cassettes in the magazine drop down by gravity. Thus, with three cassettes in the tunnel the injection of the next cassette moves the forward cassette a distance which is limited by Part 10. Then, as the handle is withdrawn, the leading exposed cassette drops away. The plates are exposed during the backward motion of the handle. A switch for automatic exposure is mounted on Part 2 and its tripper on Part 1. If such a switch is not available or not used, it is quite satisfactory to permit the x-ray technician to expose the plates during the most rapid backward motion of the handle.

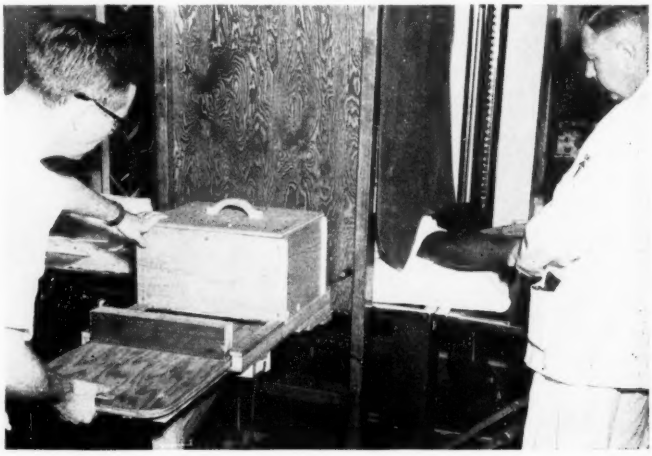

Fig. 3.—Patient is lying across apparatus on x-ray table in readiness for the injection. Operators are protected by lead plywood shield and sheet of rubberized lead.

Methods and Materials

The injection technique is essentially that described by Dotter and Steinberg.[2]

1. A Robb-Steinberg cannula or No. 13 needle is placed in preferably the antecubital vein.

2. Arm-to-tongue and arm-to-lung circulation times are done with the use of ether for the former and dehydrocholic acid (Decholin) for the latter.

3. The patient's position as shown in Figure 3 may be changed to meet special needs.

4. Preliminary scout films are taken and examined immediately before injection and corrections made as necessary in position and roentgenologic technique.

5. After preliminary sensitivity tests, 50 cc. of

70% sodium acetrizoate (Urokon) solution is injected rapidly by the intravenous route.

6. At 200 ma capacity the films should be exposed at one-tenth or one-twentieth of a second for adults, and one-twentieth of a second for children.

Summary

The construction and operation of an inexpensive rapid cassette changer for contrast studies is detailed.

The following persons aided in this study: Mr. Frank Strum, through his excellent carpentry and suggestions; Mr. Jerome L. Mathias, the Chief X-Ray Technician at Triboro Hospital; Mrs. Helen Poulos, through her art work, and M. Pikuritz through photography.

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Ischemic Necrosis of Remaining Stomach Following Subtotal Gastrectomy

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Ischemic necrosis of the remaining part of the stomach rarely occurs after subtotal gastrectomy. Only one patient with such a complication has been described in the recent surgical literature. This patient was reported by Rutter in 1953.[1] The possibility of necrosis of the gastric remnant is not mentioned in several recent textbooks of abdominal surgery.* In the patient described in this report, extensive necrosis of the gastric remnant developed after a subtotal gastrectomy had been performed for carcinoma.

Report of a Case

The patient, a 54-year-old Negro woman, was admitted to the Surgical Service of The Johns Hopkins Hospital on Oct. 22, 1954, because of intermittent epigastric pain for one year. The pain initially began after meals and was relieved by eructation; it subsequently began to appear before meals and was relieved by food. The patient's weight decreased from 170 to 150 lb. in the six months before admission. There was no hematemesis.

Physical examination showed no significant abnormalities. The patient was in a good nutritional state despite the loss of weight. The hematocrit reading was 40%. A radiologic examination of the stomach showed an extensive deformity of the antrum, which was interpreted as the result of a large infiltrating neoplasm.

A laparotomy was performed on Oct. 24, 1954, through an upper midline incision. An infiltrating lesion in the gastric antrum was biopsied and diagnosed as carcinoma by frozen section examination. A radical subtotal gastrectomy was then performed. The duodenum was divided 3 cm. distal to the pylorus. The entire gastrocolic omentum was excised. The spleen was removed with the stomach, and the left gastric artery and vein were divided near the celiac axis. Several small lymph nodes near the left gastric artery were excised. An 80% gastrectomy was performed, with the removal of most of the lesser curvature. No clamp was placed proximal to the line of division of the stomach. When the stomach was divided, it was noticed that the gastric margins bled very little. The gastric remnant became pale and mottled. A small portion of the gastrohepatic omentum near the esophagus was left attached to the lesser curvature because of the appearance of the stomach. The gastric remnant was inspected by several observers, all of whom thought that the circulation would be adequate. The lesser curvature was closed, and an antecolic gastrojejunostomy was performed with a stoma about 8 cm. in diameter. The inner suture line was a continuous suture of 00 chromic absorbable surgical (gut) suture, and the outer suture line was interrupted sutures of fine silk. The left upper quadrant was drained with a cigarette drain placed through a stab wound. The patient tolerated the three-hour operative procedure well, receiving 1 liter of blood. Pathological examination of the resected portion of the stomach showed an adenocarcinoma with metastases in six of nine lymph nodes examined.

Brown watery fluid appeared at the site of the drain in the left upper quadrant about 12 hours after operation and continued to drain in amounts sufficient to require frequent change of the dressings in the next 24 hours. The day following operation the patient complained only of moderate incisional pain. The abdomen was soft. No bowel sounds could be heard. The temperature was 99.6 F., the pulse rate 120/minute, and the blood pressure 130/70 mm.Hg. The hematocrit reading was 45%. Thirty-six hours after operation, methylene blue was injected into the stomach through a nasogastric tube and promptly appeared on the dressings at the drain site. The patient was returned to the operating room for an emergency laparotomy.

The peritoneal cavity was entered through the

Submitted for publication March 20, 1956.

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* References 2-8.

previous incision. There was no generalized peritonitis, but a local accumulation of methylene blue and bile was present in the left upper quadrant. A perforation was present in the anastomosis near the greater curvature; the stomach was gangrenous in this region. The area of gangrene was on the greater curvature and measured about 3×7 cm. It extended up to about 1 cm. from the esophagogastric junction. There was no mechanical defect in the suture line; it was felt that perforation resulted from loss of muscular tone in the necrotic stomach.

The extent of the gangrene made a total gastrectomy necessary. The jejunum was divided proximal and distal to the gastrojejunostomy, and the esophagus was divided 2 cm. above the esophagogastric junction. A Roux-Y esophagojejunostomy was constructed, with an end-to-end anastomosis between the esophagus and jejunum and an end-to-side anastomosis between the proximal and distal jejunum. The anastomoses were constructed with an inner suture line of 00 chromic absorbable surgical (gut) suture and an outer suture line of interrupted fine silk sutures. One cigarette drain was placed in the left upper quadrant. The patient tolerated the three-hour procedure well; she received 750 ml. of blood. Pathological examination of the resected gastric remnant showed a hemorrhagic infarction of the entire gastric wall along the greater curvature.

The postoperative chemotherapy included parenteral administration of penicillin and streptomycin. The patient was given water by mouth on the fourth postoperative day, and a full liquid diet was begun on the fifth postoperative day. The subsequent food intake was fairly good, although only a small amount of food could be eaten at each meal. A subphrenic infection developed by the fifth postoperative day; the patient had a temperature of 102 F, purulent drainage from the site of the drain, and a small left pleural effusion. The infection responded to chemotherapy with oxytetracycline (Terramycin) and erythromycin; the patient became afebrile by the 16th postoperative day, and was discharged on the 23d postoperative day. The patient weighed 142 lb. when discharged from the hospital.

The patient has been followed in the Gastroenterology Clinic by Dr. Moses Paulsen. She has eaten a high caloric, high protein diet in three to six feedings a day. Her weight has remained near 130 lb. for the past several months. The patient has felt well. The only complaints are a feeling of fullness when a large meal is taken and an infrequent epigastric burning sensation. Her diet has been supplemented with vitamins, including vitamin B_{12}, and ferrous gluconate. There is no sign of recurrence of the gastric neoplasm one year after operation.

Comment

Collateral Circulation of the Stomach.—Ischemic necrosis of the stomach is uncommon because the stomach is richly supplied with blood vessels that freely anastomose with one another. The submucous arterial plexus of the stomach is a pathway through which blood can easily flow between any two areas of the stomach. Two recent papers have emphasized the extent of the gastric collateral circulation. Brown and Derr studied arterial circulation of 20 stomachs by the injection of radiopaque dyes.[9] In each experiment the injected material readily diffused throughout the entire stomach. Similar results were obtained from injection studies performed by Barlow, Bentley, and Walder.[10] Both groups of authors emphasized the absence of end-arteries in the stomach as being due to the extent of the submucous arterial plexus.

The abundant collateral circulation of the stomach has also been illustrated through experimental attempts to reduce gastric acidity by reduction of the gastric blood supply. Bernheim, in 1932, found that ligation of all four of the major arteries of the stomach in dogs resulted in gangrene of the midportion of the stomach.[11] Less extensive ligations did not significantly reduce gastric acidity. Similar results were obtained by Layne and Bergh[12] and Babkin, Armour, and Webster[13] in 1943, by Le Veen[14] in 1948, and by Holm and coworkers[15] in 1949. Baronofsky did not find that devascularization of the stomach in the dog provided any protection against peptic ulcer produced by histamine injection.[16] In India, Somervell reported an extensive experience with the treatment of peptic ulcer by reduction of the blood supply of the stomach, but good results have not been obtained by other surgeons.[17] The difference in results may be due to two characteristics of the group of patients treated by Somervell. As a concomitant gastroenterostomy was performed in most

patients, the results obtained were not due solely to the vascular ligation. Also, patients were operated on who might have responded to medical therapy; as economic circumstances prevented adequate medical therapy, surgical therapy was carried out in all patients.

Clinical experiences with gastric surgery have emphasized the resistance of the stomach to ischemic necrosis. Visick described a "measured radical gastrectomy" in over 200 patients.[18] Either all or all but one of the vasa brevia were divided. The remaining stomach consisted of a small "devascularized" remnant measuring 1.5 in. along the lesser curvature and 3 in. along the greater curvature. No color changes were noted in the gastric remnant. Necrosis of the stomach did not develop in any patient. Hinton and Localio treated 13 patients with a gastric ulcer near the esophagogastric junction.[19] A subtotal gastrectomy was performed by mobilizing the lesser curvature to the esophagus and the greater curvature above the entrance of the short gastric vessels. None of their patients had any demonstrable circulatory impairment of the remaining stomach. Wangensteen has performed an extensive gastric resection in which a gastric remnant representing 5% to 10% of the stomach was anastomosed to the pyloric antrum.[20] The spleen was removed in all patients with a history of hemorrhage. The greater and lesser curvatures were mobilized completely, except for one or two vessels on the posterior gastric wall. In some patients the only blood supply to the gastric remnant was from the esophagus. There was no evidence of circulatory impairment in any patient.

A personal inquiry was made of five surgeons who have had extensive experience in gastric surgery.† Two of the surgeons (Drs. Crile and Wangensteen) had each seen two patients with ischemic necrosis of the gastric remnant; three of these four patients had had a ligation of the left gastric artery and a splenectomy. The other three surgeons (Drs. Harkins, Marshall, and Walters) had not encountered this complication. A recent communication from Dr. Julian Quattlebaum,‡ of Savannah, Ga., reported that two patients had developed necrosis of the gastric remnant following radical subtotal gastrectomy with splenectomy and ligation of the left gastric artery. Marked pallor of the gastric remnant was noted at operation in one patient.

Characteristics of Necrosis of Gastric Remnant.—The anatomical, experimental, and clinical observations of the gastric circulation summarized in the preceding section provide adequate explanation of the infrequent occurrence of gastric necrosis following subtotal gastrectomy. However, there is no satisfactory explanation of the development of necrosis in the patient reported on here or in the one reported on by Rutter,[1] other than the decrease in blood supply resulting from ligation of the left gastric artery and division of most of the blood vessels along the greater curvature of the stomach.

In the patient reported on here, all the vasa brevia were divided on the greater curvature, but a few vessels on the lesser curvature near the esophagus were not divided. The pale, mottled appearance that developed in the gastric remnant probably was an indication of inadequate blood supply. Similar color changes were not observed by Wangensteen,[20] Hinton and Localio,[19] or Visick.[18] The significant postoperative event was the drainage of brown watery fluid from the site of the drain, beginning 12 hours after operation and progressively increasing in amount. The patient's general condition at this time was satisfactory; therefore, the diagnosis would not have been made if the draining fluid had not suggested the instillation of methylene blue into the stomach. The fact that the necrosis extended to the esophagus indicates

† Crile, G.; Harkins, H. N.; Marshall, S. F.; Walters, W., and Wangensteen, O. H.: Personal communications to the author, 1956.

‡ Quattlebaum, J., Personal communication to the author, 1956.

that no significant blood supply came to the stomach from the esophagus.

The patient reported on by Rutter [1] had a subtotal gastrectomy performed in which the left gastric artery was ligated and the greater curvature extensively mobilized in order to do a gastroduodenostomy. No color change was observed in the gastric remnant, but severe symptoms appeared in less than 24 hours after operation. Fluid appeared at the drain site on the third postoperative day. The good general condition of the patient, however, delayed laparotomy until the ninth postoperative day. The entire gastric remnant was necrotic. A resection did not seem possible; death occurred two days later.

The postoperative course of these two patients would suggest that definite color changes in the gastric remnant should be given serious consideration. A drain inserted near the gastric remnant may provide information that will make a diagnosis of gastric necrosis possible in the early postoperative period. Abdominal exploration should not be postponed because of the absence of signs of generalized peritonitis. The danger of necrosis of the gastric remnant would seem to be greatest in operations in which the left gastric artery is ligated and a splenectomy performed.

Comment

A patient is reported on who had a radical subtotal gastrectomy performed for carcinoma of the stomach. Inadequate circulation to the remaining stomach was suspected because the stomach became pale and mottled in appearance. Brown watery fluid appeared about a drain in the left upper quadrant about 12 hours after operation. A perforation of the anastomosis was proved by placing methylene blue in the stomach and noting its appearance at the drain site. Extensive necrosis of the gastric remnant was found when the abdomen was opened about 40 hours after the gastrectomy had been performed. The necrotic stomach was excised and an esophagojejunostomy performed. The patient is doing well one year after operation.

Only one other case of necrosis of the gastric remnant following subtotal gastrectomy was found in the recent surgical literature. There was no adequate explanation for the necrosis of the stomach in either case, other than ligation of the left gastric artery and division of most of the blood vessels along the greater curvature of the stomach. The significant clinical features of the two cases included a color change in the gastric remnant in one patient, the appearance of symptoms in the early postoperative period, and the absence of signs of generalized peritonitis. Personal inquiries of six surgeons with extensive experiences in gastric surgery revealed that a total of six patients with such a complication had been encountered; the subtotal gastrectomy in most of these patients had included ligation of the left gastric artery and a concomitant splenectomy.

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Acroparesthesia

A Symptom of Median Nerve Compression at the Wrist

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In 1953, Kremer, Gilliatt, Golding, and Wilson [1] reported a series of cases of acroparesthesia in which, acting on a suggestion of McArdle,[2] they had divided the transverse carpal ligament, thus decompressing the median nerve. This procedure resulted in immediate relief in most instances. Our purpose here is to describe a number of cases of this common disorder in which this procedure has been done, review the background of our knowledge of the condition, and relate it to the better-known syndrome of median nerve compression in the carpal tunnel.

Acroparesthesia is quite stereotyped in its clinical manifestations. Although much commoner in women, and indeed characteristically described in the sex, it may occur in men. The main complaint is of paresthesias in the hands. These, while they may be bilateral, are frequently more marked in the hand more used. The description varies: Often a numbness is present, sometimes a painful tingling or burning in the finger tips. These symptoms occur only at night, awaken the patient from sleep, and are relieved by getting up and walking about or shaking the arm at the side of the bed. They recur several times a night. In the morning, the fingers feel numb and clumsy, and for a short period there is difficulty in handling small objects. Questioning usually elicits a story of stiffness of the fingers, particularly in flexion; the patient describes a sensation of tightness, and sometimes actual swelling is shown by inability to remove a ring. In the early stages the symptoms are usually mild. During the day, no disability is noted except on repeated use of the hands, when some stiffness and awkwardness occur. A dull ache, usually along the flexor aspect of the forearm, rarely extending up to the shoulder, is often present.

The symptoms are likely to occur in pregnancy or at the menopause. In the former situation they may disappear after term, only to return with subsequent pregnancies. In time, the increasing frequency and severity of the symptoms lead to a search for help, although some few patients are so distressed from the beginning that medical advice is sought early. The results of physical examination are usually completely normal at this time.

This syndrome has been familiar since Schultze named it in 1893. Wartenberg,[3] commenting on the constant pattern, said, "It is so outspoken in features and course that it constitutes a definite clinical entity," and mentioned a trilogy of acroparesthesia characterized by "transient paresthesiae exclusively during the night, absence of any signs, and a long, benign, self-limited course." At first, it was considered a vasomotor disturbance, a functional neurosis, or a manifestation of root compression. Both Walshe [4] and Wartenberg [3] have postulated a disturbance of the neurovascular bundle at the thoracic outlet. The former noted an increased frequency during the war in England and remarked that it was seen in "women, normally unaccustomed to full housework, who, under wartime circumstances, had been obliged to undertake the entire work of their homes."

While neurologists were familiar with acroparesthesia, others were aware of com-

Submitted for publication Feb. 28, 1956.

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pression of the median nerve due to lesions at the wrist. Sir James Paget, in 1865, described delayed median nerve palsy in a patient with an old fracture of the wrist, and Abbott and Saunders[5] were able to collect a number of such cases. Kanavel,[6] in his classic paper on tuberculous tenosynovitis of the hand, pointed out that attention should be drawn particularly to involvement of the median nerve. The manifestations which he described were numbness, tingling, and burning pain, particularly at night; one of his patients frequently got up to seek relief by immersing her hand in hot water. Objective signs of median nerve dysfunction were, however, lacking.

Cases of tardy median palsy occurying in acromegalics have been described,* and it is significant that note has been made of severe nocturnal pains, relief from which was obtained only by suspending the hands over the bar of the bed.

However, the first report dealing with spontaneous compression of the median nerve in the carpal tunnel was that of Moersch,[11] who suggested section of the transverse carpal ligament. Cannon and Love[12] presented a number of cases showing varying degrees of atrophy of the lateral aspect of the thenar eminence with paresthesias and sensory loss in the median distribution. This was followed by other reports,† in all of which nocturnal exacerbation of symptoms was noted.

To McArdle[2] must go the credit for recognizing the essential similarity of the early symptomatology of median nerve compression at the wrist to the acroparesthetic syndrome, the difference lying only in the presence of physical signs of median nerve dysfunction in the former and their absence, even after many years, in the latter. That late thenar atrophy was known in acroparesthesia, however, is shown by the report of Abrahamson,[17] who, at a meeting of the New York Neurological Society on Nov. 1, 1904, described the case of a 52-year-old woman who complained of numbness and paresthesias in both hands, mostly at night. There was marked symmetrical atrophy of both thenar eminences. He is quoted as regarding this case as one of acroparesthesia with subsequent atrophy.

Report of Cases

Sixteen cases of acroparesthesia have been seen. Of these, operation has been undertaken in 9, involving section of the transverse carpal ligament in 12 hands. The selected case reports illustrate some significant features of the disorder.

Case 1.—A 35-year-old, left-handed woman was admitted to Colorado General Hospital on Sept. 26, 1955. Her complaint was of pain and burning paresthesias of the fingers of the left hand. These had been present in a mild form for about seven weeks, but during the last week she had been awakened several times nightly with excruciating burning and tingling in all fingers of the left hand, accompanied by a sensation of swelling of the fingers. She would get out of bed, walk about, and rub the arm, and finally the symptoms would abate, only to recur later on during the night. Recourse to narcotics had become necessary. Her paresthesias could be reproduced in the four fingers of the left hand by occluding the circulation, and crepitus was heard upon auscultation of the wrist during flexion movements of the fingers. There were no abnormal neurological signs.

At operation the left transverse carpal ligament was completely divided. Relief was dramatic, and symptoms have not returned.

Comment.—Acute forms of acroparesthesia in which symptoms are so severe and insistent that relief is sought at once were known to Oppenheim[18] but have received little attention in the literature since.

Case 2.—A 46-year-old man was admitted to the hospital on April 4, 1955. He had been a baker for 30 years, and the kneading of dough and use of a rolling pin involved hours of flexion and extension movements of the wrists. For the last 10 years, he had been moderately, and at times severely, disabled by paresthesias which occurred in both hands, more on the left, more in the fingers supplied by the median nerve, and always at night. First thing in the morning, his fingers were a little clumsy, but this would wear off and he would be able to carry on his work with only occasional tingling. However, three to five times

* References 7-10.

† References 13-16.

a night he would waken with pain in his forearms and a numb, cold feeling in the fingers which caused him to get out of bed to seek relief. For the last nine months, he had been unable to work as a result of the severity of these symptoms. There were no abnormal physical signs in the nervous system.

On April 18, 1955, the left transverse carpal ligament was divided, and on April 24, 1955, a similar operation was done on the right. On each side, the median nerve was seen to be blue-gray and lusterless beneath the distal part of the ligament. Immediate relief resulted from the surgery, and to date he has had no recurrence and has been able to follow his occupation.

Comment.—The significant features in this case are the sex and occupation of the patient, the very long duration without any physical signs, and the considerable difficulty which accrued as a result of the symptoms.

CASE 3.—A 36-year-old butcher was admitted to the hospital on Jan. 5, 1955, complaining of pain and numbness of both hands for 10 years. The symptoms were equally marked in both hands, particularly after a hard day's work, and consistently awakened him around 4 o'clock in the morning. The paresthesias occurred in all fingers of both hands and were relieved by his getting up and walking about. On arising in the morning, he noticed swelling of the fingers so that he could not remove a ring, and dull, aching pain was present along the ulnar aspect of both forearms. As the day progressed, all symptoms disappeared. In 1947, a right scalenotomy had been performed without giving relief.

Physical examination revealed no abnormalities, except for diminution of the radial pulses upon hyperabduction of the arms. X-ray studies showed a well-developed cervical rib on the right and a rudimentary one on the left, both arising from the seventh cervical vertebra.

On Jan. 14, 1955, the right transverse carpal ligament was divided. The symptoms were immediately relieved. On March 1, 1955, the left transverse carpal ligament was divided, and although this resulted in some relief, pain along the ulnar border of the forearm and paresthesia continued to waken him at night as before. On April 4, 1955, the wound was reopened, and it was found that complete division of the transverse carpal ligament had not been achieved; the remainder of the ligament was divided, and the median nerve was seen to be completely free. Since that date the patient has had no further symptoms.

Comment.—Confusion may occur with the so-called hyperabduction syndrome; however, perusal of the literature on this subject has not given rise in our minds to any precise concept of the clinical picture. The sex and occupation of this patient should be noted. The long period of disability was not altered by the scalenotomy which had been performed previously on the evidence presented by radiographic examination of the neck.

CASE 4.—A 31-year-old woman was admitted to the hospital in July, 1955. A diagnosis of acromegaly had been established in 1954, and it was thought that this condition had been present for at least four years. Her admission was occasioned by the occurrence of severe, burning paresthesias in both hands during the night only. She would wake up three or four times each night, hang her arms over the side of the bed, and shake them for a few minutes until relief was obtained. She noted that the symptoms were much worse in the thumb and in the index and middle fingers of the right hand, and that even during the day these fingers felt numb.

Examination, in addition to revealing the typical features of acromegaly, showed wasting and appropriate weakness of both the short abductor and the opponens of the thumb on the right side. No sensory loss was noted.

On Aug. 7, 1955, the transverse carpal ligament was divided on the right. The median nerve was found to be greatly enlarged. There was immediate and complete relief of the symptoms referable to the right hand. She has recently asked that operation be done on the left.

Comment.—This case illustrates very well the occurrence of strictly nocturnal paresthesias in a patient with a tardy median palsy associated with acromegaly.

CASE 5.—A 56-year-old woman was awakened one night in July, 1955, with burning, aching pain in the first three fingers and the thumb of the right hand. After this, she experienced the same symptoms nightly and would frequently have to get out of bed to obtain relief. Two months later she observed that her hands were growing stiff, and before long she was unable to flex the distal interphalangeal joint of either thumb.

There were no abnormal physical signs referable to the nervous system. On both sides there was tenderness along the course of the tendon of the flexor pollicis longus, and the range of flexion of the distal interphalangeal joint of the thumb was limited in both active and passive movement. A

local enlargement of the tendon was palpated at the base of the thumb, and this was considered responsible for the locking. Crepitus was present on flexion of the fingers.

At operation on Oct. 21, 1955, the right transverse carpal ligament was divided. The median nerve was seen to be cyanotic and lusterless beneath the transverse carpal ligament. The tendon sheath of the flexor pollicis longus was found to be thickened and adherent to the median nerve. There has been no recurrence of acroparesthesia. On Dec. 7, 1955, surgical correction of the tendon sheath disorder was undertaken.

Comment.—This case illustrates the concurrence of tenosynovitis of the flexor tendons and compression of the median nerve, a relationship observed by Michaelis,[19] Phalen and co-workers,[15] and Vicale and Scarff[20] and considered by the last authors and by McKee[21] to be of causal significance even when frank clinical evidence of tendon sheath involvement is lacking. The latter situation is illustrated in the following case reports:

Case 6.—This 23-year-old man was admitted to Colorado General Hospital on Nov. 23, 1955. He was a rancher, and for many years had milked at least 15 cows twice daily. For the last 10 years, he had had pain in the thenar eminence on the right side, extending up the forearm and occasionally up to the shoulder. This pain might occur after he had been milking the cows, but more frequently it would waken him in the early hours of the morning, when, in addition, he would have paresthesias in the fingers of the right hand.

Examination showed no abnormal neurological signs. Harsh crepitus was heard over the flexor tendons when the fingers were flexed. In February, 1955, he had had a right scalenotomy without relief.

The transverse carpal ligament was divided on Nov. 25, 1955. The flexor tendon sheaths were considerably thickened, and a biopsy showed excess collagenous connective tissue.

This patient has had no further nocturnal paresthesias and is very much improved. He still, however, complains of some stiffness of his fingers, particularly in the morning; this is increased by use of them during his work.

Comment.—This is a somewhat atypical case illustrating one of the variants that may occur. The principal complaint was of pain in the right thenar muscles and stiffness in the hands. These symptoms so dominated the picture that paresthesia did not seem a major complaint.

Case 7.—A married woman of 31 years began to experience nocturnal burning and tingling in the fingers of the right hand three years before being seen. At first, symptoms were present only during summer months when she was gardening, but more recently she had had them in the winter as well. Her symptoms were made worse by knitting and other activities in which she used the hand. She sometimes experienced subjective numbness in the distribution of the median nerve during activities involving wrist and finger movements.

The patient's maternal grandfather, who was left-handed, suffered from acroparesthesia on the left, and her mother has had symptoms on the right, her dominant hand, to the extent that she has not had a full night's sleep in 15 years.

Apart from crepitus during finger flexion, physical examination was noncontributory.

On Jan. 19, 1956, the right transverse carpal ligament was divided. The median nerve was found to be bound down to the thickened tendon sheaths beneath it. There were some blue-gray coloring and loss of luster of the nerve beneath the ligament.

Comment.—The family history in this case is worthy of note. Familial incidence has not been emphasized in the literature. Lateralization of symptoms in members of this family to the dominant hand again emphasizes the tendency for occurrence in the hand more used.

Technique of Operation

If adequate uncovering of the median nerve is to be effected, the transverse carpal ligament must be divided under direct vision. The transverse incision in the flexor crease of the wrist does not afford sufficient exposure to insure that no fibers remain uncut.

It is better to incise in or parallel to the crease at the base of the thenar eminence and carry this incision to the radial side of the flexor creases at the wrist before turning to the volar surface of the forearm. The flap thus formed is turned back, and the median nerve is identified. The transverse carpal ligament is then divided under direct vision, beginning proximally and proceeding

distally until all fibers have been cut and a finger can be passed along the median nerve into the palm of the hand.

Comment

Speculation as to the etiology of this well-known syndrome has been both frequent and unfruitful. Evidence has accumulated that it is due to compression of the median nerve at the wrist and that the precipitating factor, far from being progressive lowering of the shoulder girdle, is, in fact, an increase in the volume of the structures passing through the carpal tunnel. This increase may be due to thickening of the flexor sheaths as in frank tenosynovitis or to the presence of an enlarged nerve as has been described in acromegaly. The frequency with which symptoms occur in patients whose occupations involve repeated flexion-extension movements of the wrist or fingers is illustrated by the present series which includes a butcher, a baker, and a rancher. In addition, it has been seen in a pianist and in several women forced to undertake heavy housework to which they were unaccustomed.

Kendall,[14] discussing tardy median palsies, noted the occupational incidence and thought that, in addition to repeated wrist extension, it was necessary to postulate another factor. He found that if the fingers were flexed at the same time as the wrist was extended the median nerve became liable to considerable friction, and he held this responsible for the resulting tardy palsy. Another possibility is the concurrence of tenosynovitis, and while this view rests on a firm pathological basis in relatively few cases, it is suggested by the morning stiffness and swelling of the fingers, so characteristic of acroparesthesia, and by the operative findings in our own and other cases. Auscultation over the tendons during flexion may be useful, since in a number of cases crepitus has been heard. Kremer and co-workers[1] found difficulty in explaining the frequent association of pain along the flexor aspect of the forearm, and postulated a spread to the cutaneous areas supplied by those segments which are included in the median nerve. In those cases with frank tenosynovitis, it is a prominent symptom and merely reflects the presence of that condition.

The confusion with cervical rib syndrome is illustrated by the two cases reported here in which scalenotomy had previously been undertaken. When neurological difficulties arise from the presence of this anomaly, involvement of seventh and eighth roots would be expected, and this is indeed the usual finding. Wilson[22] described cases of cervical rib in which wasting of those muscles of the thenar eminence supplied by the median nerve occurred and spoke of this as "a particular amyotrophy . . . of great diagnostic value," stating that, though the nerve fibers concerned run distally in the median nerve, their presumptive radicular origin is from the seventh or eighth root, in which case they must occupy a fixed site among the constituent fasciculi in relation to the rib. It would seem that here, too, the presence of a cervical rib has led to false conclusions regarding the segmental innervation of the thenar muscles as well as the role of the rib in producing symptoms. As for the "scalenus anticus syndrome," the very existence of this entity is in doubt, and the *sine qua non* for diagnosis, the presence of tenderness on pressure over the insertion of the muscle, is invariable in the normal subject.

Summary

Acroparesthesia is a common and distressing disorder manifested by nocturnal tingling and burning in the fingers resulting from compression of the median nerve as it enters the hand. Of the various causes, tenosynovitis of flexor tendons is common. Uncovering the nerve by dividing the transverse carpal ligament results in immediate relief.

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Hemorrhage as a Complication of Common Duct Stones

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Intrinsic bleeding from the common bile duct consequent to erosion of a blood vessel by a stone is a relatively infrequent-occurring entity, but its infrequency and, still more, the difficulty of common duct investigation combine to make its diagnosis difficult even after profuse hemorrhage supervenes. The immediate precipitating factor responsible for the bleeding is no doubt an erosion into a blood vessel by an overlying stone. Loss of blood may be trivial if the vessel is affected by some pathological process, or severe if it is normal. We [5] previously reported two cases of massive bleeding from the common bile duct produced as a result of irritation of the ductal mucosa by an indwelling T-tube. A similar instance with fatal hemorrhage from choledochal bleeding was reported by Campbell.[1] In Campbell's case intracholedochal intubation was responsible for the ulceration into and hemorrhage from the posterior superior pancreaticoduodenal artery. White and Jankelson [7] and Hudson and Johnson [4] reported cases of gall-bladder bleeding associated with cholelithiasis. The latter authors state that many cases of unexplained secondary anemia or of blood in the stools are due to cholelithiasis. Choledochal bleeding resulting from erosion of a blood vessel by a stone is one of the very rare complications of biliary disease. Although stones in the bile passages are not uncommon occurrences, very few instances have been known where the stones provoked hemorrhages. Perusal of the literature also suggests that ductal bleeding resulting from any cause is very rare, and that due to stones is most unusual. The reason may be that the majority of such cases show little or no clinical findings and that the isolated case is not published. However, choledochal bleeding is regarded as one of the less frequent occurrences, and references to such an event are rare.

Not infrequently the clinician is presented with a patient devoid of localizing signs and in whom it is difficult or impossible to render a definite clinical diagnosis of choledochal bleeding. The case descriptions which follow confirm this view; the true diagnosis was unsuspected in all of these patients until it was reached at laparotomy.

Our interest in this subject was stimulated by the opportunity to participate in the treatment of three patients with choledochal hemorrhage induced by ulceration of a blood vessel by a stone. The clinical material covered in this report was obtained from these three patients. The cases described below are of interest mainly because of the difficulty in diagnosis, the etiology, and the treatment.

Report of Cases

CASE 1.—The patient was a man of 51 who was in good health until he presented himself at the office on Oct. 15, 1955, with a six weeks' history of gastric flatulence, weakness, and a feeling of abdominal distention. These symptoms were unrelated to food, and examination revealed no abnormal physical signs. Further interrogation of the patient elicited the fact that his stools were of dark-black color for the past few months, although he had eaten no food and had partaken of no medication that would discolor the stools

Submitted for publication Jan. 25, 1956.

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Examination of the gastrointestinal tract with the aid of a barium meal showed distortion of the duodenal cap suggestive of ulcer formation; no definite niche could be demonstrated, however, in any of the films. The stools were tarry and gave a positive test for occult blood.

Conservative therapy was instituted at first; the patient was given a bland diet and antispasmotics for the relief of the abdominal pain and discomfort. There followed very little improvement in symptoms in spite of strict adherence to diet and medication.

On the night before admission to Adelphi Hospital, Brooklyn, the patient suddenly developed acute abdominal pain with dizziness, weakness, and a sensation of feeling faint. He vomited profuse amounts of coffee-ground material mixed with fresh blood; he also passed large amounts of black, fluid stools.

On admission to the hospital the patient appeared acutely ill. The temperature was 100 F, pulse rate 110, and respirations 24. The blood pressure was 105/60. Abdominal examination revealed no significant findings. Blood analysis disclosed a marked secondary anemia, with 2,800,000 red blood cells per cubic millimeter and 55% hemoglobin. The white blood cell count was 12,500 per cubic millimeter, with normal distribution of cells. The stools gave a very strongly positive test for blood. The clinical impression was that the patient was suffering from an actively bleeding duodenal ulcer.

The patient was transfused with 1000 cc. of whole blood, following which he made a fairly rapid recovery. Operation was then advised mainly on account of the hemorrhage and the possibility that the bleeding might recur. After suitable preparation operation was undertaken for resection of the stomach and ulcerated duodenum.

Laparotomy through an upper midline incision was carried out, and the whole of the abdominal viscera was explored. There was no gross evidence of disease in the stomach, duodenum, or small or large intestine aside from dense adhesions between the gall bladder and duodenum.

The gall bladder was thick-walled, and its cavity contained numerous calculi. The common bile duct was widely dilated, and on palpation a number of stones could be felt within its lumen. When it was opened, there was found, in addition to the stones, some fresh blood.

A cholecystectomy was done followed by removal of the stones from the bile duct. One large stone was found impacted against the wall of the duct; when it was dislodged and extracted, there followed a gush of blood. Bleeding was readily controlled, however, by digital pressure. Examination of the lumen of the duct at this time revealed the presence of a large varix in the mucosa; the wall of the varix was ulcerated and bleeding. It was quite evident that the hemorrhage in this case was a result of erosion of the thin-walled vein by the overlying impacted stone.

The dilated vein was tied with a suture ligature placed around it, and the opening in the duct was closed tightly. No attempt was made to drain the common bile duct for fear that an indwelling tube might provoke bleeding. A cigarette drain was placed, however, in Morison's pouch, and the abdominal wall was closed in layers; there followed an uneventful recovery. The patient has been free from symptoms since the operation.

Case 2.—The patient was a 48-year-old woman who was admitted to Mount Royal Hospital, Montreal, on April 12, 1948, with a history of sharp pain in the epigastrium radiating also to the back, for the previous 36 hours. She had experienced many mild attacks of similar pain over the last 8 or 10 months, but none had been as severe as that which led to her admission to the hospital. There had been nausea but no vomiting. The bowels had been open on the day of admission, and the stools were noted to be dark black. She stated that the stools were black on several previous occasions during the past few weeks. There was a moderate degree of weight loss, although her appetite was not too bad.

The patient had had a cholecystectomy done 18 months previously because of gall-bladder disease and stones. She was in good health following the operation until the present onset of symptoms, eight months previously.

On admission to the hospital the patient appeared to be in considerable pain. The temperature was 99.8 F, pulse rate 90, and respirations 22. Blood pressure was 140/90. There was a definite icterus of the sclerae and a light jaundice of the skin. The abdomen showed marked tenderness in the right upper quadrant. There was no muscle spasm or rigidity, and no masses or organs could be palpated. The red blood cells numbered 3,500,000 per cubic millimeter, with 70% hemoglobin. The white blood cell count was 9800 per cubic millimeter, with a normal distribution of the cells. The urine showed the presence of bile, and the stools were acholic and gave a strongly positive test for occult blood. The icterus index was elevated to 26. Radiograms of the gastrointestinal tract revealed no abnormal findings. The clinical impression was that the patient had a common duct stone causing obstruction and jaundice. The cause of the blood in the stools could not be ascertained.

After adequate preparation of the patient, operation was undertaken for the removal of the obstruction and relief of jaundice. Laparotomy disclosed a normal stomach, duodenum, and small and large intestine. Numerous dense adhesions

were encountered around the liver and duodenum. The gall bladder was absent, having been previously removed. The common bile duct was considerably dilated and approached in size almost that of the duodenum; when opened, it was found to contain numerous small and large calculi. The mucosa of the duct was ulcerated at one point and covered by a small, adherent blood clot. When the clot was wiped away, bleeding began from the denuded mucosa; this was readily controlled by pressure. No other source of bleeding could be found in the duct or elsewhere in the gastrointestinal tract.

After removal of all stones from the bile duct the exploratory incision made in its wall was closed tightly with interrupted chromic 00 sutures. The duct was not drained for fear that an indwelling tube would irritate the eroded mucosa and promote bleeding. A cigarette drain was placed in Morison's pouch, and the abdominal wall was closed in layers. The patient made a good postoperative recovery. She has been free from symptoms and enjoying good health since the date of operation.

CASE 3.—The patient was a 52-year-old white man who was admitted to Adelphi Hospital, Brooklyn, on the morning of Feb. 10, 1953, with a 12-hour history of severe colicky pain in the right upper abdomen, accompanied by nausea and vomiting of dark, coffee-ground material mixed with blood. His previous history included an operation for removal of a gangrenous gall bladder two years before. He had been in apparent good health following the operation, but lately he had been suffering from attacks of abdominal distress, weakness, loss of appetite, and loss of weight.

On admission to the hospital the patient was in obviously severe pain, and, when first seen, he was lying in bed holding his abdomen and having frequent spasms of colic in the upper abdomen. His temperature was 99.6 F, pulse rate 94, and respirations 28; blood pressure was 110/85. There was a generalized deep jaundice of the skin and sclerae. Abdominal examination showed a right subcostal scar. The abdomen was exquisitely tender throughout, but more particularly so in the right upper quadrant. No abdominal masses could be palpated.

Laboratory Data.—Blood cell count showed 3,200,000 red blood cells per cubic millimeter, 10,200 white blood cells per cubic millimeter, and 68% hemoglobin. The blood chemistry, which included glucose, urea, cholesterol, cholesterol esters, and proteins, was within normal limits. The icterus index was 17.7, bilirubin 4.45 mg. per 100 cc., and alkaline phosphatase 8.6 units per 100 cc. Uribilinogen was positive in dilution 1:200. The urine contained bile, and the stools were tarry and gave a strongly positive reaction for blood. Radiologic examination of the gastrointestinal tract showed nothing abnormal.

In view of the previous history of cholecystectomy and the sudden onset of the abdominal pain on this occasion, considered with the findings of jaundice on clinical examination, a provisional diagnosis of common duct stone was made. The diagnosis was further substantiated by the laboratory findings of an elevated icterus index, bile in the urine, and acholic stools. The cause of the hematemesis and melena could not be very well ascertained.

At operation the stomach, duodenum, and small and large intestine appeared quite normal and showed no evidence of disease or bleeding. The common bile duct was hidden from view by dense adhesions, which, when cleared, exposed a very markedly dilated tubular structure filled with calculi of various sizes and shapes.

The common bile duct was first aspirated with a fine needle and was found to contain blood. When it was opened through a small incision and explored, the lumen was found to be filled with stones, in addition to some fresh blood. One very large stone was found to occlude the distal end of the common bile duct. When it was removed, there followed immediately a profuse hemorrhage from the common duct. The exact point of bleeding in the duct could not be visualized because of its distant location. Digital compression of the wall of the duct proved ineffective in controlling the bleeding. The common bile duct was therefore mobilized along its distal portion; a good-sized vessel was found to cross the front of the supraduodenal path of the duct. The vessel was ligated, and there followed a rapid cessation of the bleeding. A short-arm T-tube was then placed in the duct and the abdominal wall was closed in layers; recovery was uneventful. At the time of writing, almost three years since the operation, the patient is well and free from symptoms.

Evaluation

Hemorrhage of whatever source always presents a surgical challenge, and a condition as treacherous as bleeding from the common bile duct is no exception. It has already been stated in the introduction that choledochal bleeding is exceedingly rare. A review of the literature has shown that the condition has been scantily recorded, and we have been unable to find any record of a large series of cases bearing on this subject. The onset of bleeding may be slow and insidious and with very little loss of blood. Such bleeding is detected clinically

when there is a mild degree of secondary anemia, and when chemical analysis of the stools discloses the presence of occult blood. On the other hand, the onset of bleeding may be dramatic and sudden and the hemorrhage profuse. The general condition of the patient varies with the amount and rapidity of the blood loss. A patient having lost a small amount of blood may have mild symptoms and is relatively in good health. At the other extreme is a patient who presents the clinical features of profound hemorrhage and a picture of shock. In the intermediate group are patients in whom the symptomatic effects of the bleeding are not severe but who often have latent manifestations of hemorrhage which can be detected only by careful search or by special clinical investigations; the assessment of the patient may be misleading if this is not remembered. The gravity of the condition, as judged both subjectively and objectively, is directly related to the severity and duration of the bleeding.

In evaluating the findings in this series, one of the interesting facts that is brought to light is the disclosure of blood in the gastrointestinal tract in the absence of clinical signs of bleeding in that system. The difficulty in diagnosis is emphasized by all writers on the subject, and it would appear that no case was diagnosed before operation or autopsy. It may be safely stated that in the absence of local findings in the alimentary tract attention should be drawn to the biliary passages as a possible source of bleeding in all cases of occult loss of blood. Since ductal bleeding of whatever cause is very rare, its occurrence in this system attracts great interest. The difficulties encountered in the investigation of biliary tract disorders are unsurmountable. It was our object, therefore, in describing the above three cases to draw from personal experience certain conclusions about the clinical aspect of this unusual complication.

The symptoms presented by our group of patients were rather distinctive of biliary tract disease with gastrointestinal hemorrhage, although in the first case the clinical impression was that the patient was suffering from an actively bleeding duodenal ulcer. Analysis of the diagnostic facts relating to this disease complex shows that pain was the most important subjective symptom. All our patients had acute abdominal pain directed primarily to the right upper quadrant. The onset of symptoms which led to the patients' admission to the hospital was acute in all three instances. The duration of symptoms before operation varied from six weeks to eight months. The character of the pain varied from sharp to colicky. Nausea and vomiting occurred in two patients, and nausea alone in the third. The vomitus in the two patients consisted of coffee-ground material mixed with fresh blood. Tarry stools was a common finding in all three patients. Two of the patients had undergone previous cholecystectomy for cholecystitis and cholelithiasis. In one patient the cholecystectomy was done because of a gangrenous gall bladder.

The ages of the patients in this group ranged from 48 to 52 years, with an average of 50 years. This age group follows the usual pattern recorded in large statistical analyses dealing with cholecystitis, cholelithiasis, and choledocholithiasis. Two of the patients were male and one female. Although the present group of cases is too small for statistical evaluation, it nevertheless points to the fact that the complication described is more prevalent among male patients. One of us (J. R.)[6] has previously shown the high incidence of impacted calculi in the gall bladder of males as compared with females.

Physical examination of all three patients revealed well-developed and well-nourished persons. The temperature was slightly elevated above normal in all instances. Jaundice of the sclerae and skin was present in two patients. There were tenderness, release pain, and spasticity of the right upper abdomen in all patients. A moderate degree of secondary anemia was evident in every instance. The red blood cell count ranged

from 2,800,000 to 3,500,000 per cubic millimeter, and the hemoglobin from 55% to 70%. The white blood cell count was only slightly elevated, averaging 10,800 per cubic millimeter. The differential count showed normal distribution of its cellular components. Tarry stools which gave a strongly positive test for occult blood were noted in every instance. Radiograms of the gastrointestinal tract were suggestive of a duodenal ulcer in one patient, and in the two others it proved normal.

The preoperative diagnosis was that of common duct obstruction caused by a calculus, in two patients; in one patient the clinical impression was that of an actively bleeding duodenal ulcer. The cause of the bleeding was not determined in any of the patients preoperatively.

At operation, all three patients presented a rather unique anatomic picture. In each instance the common bile duct was widely dilated and filled with calculi and some fresh blood. In two patients the gall bladder had been previously removed; in the remaining patient the gall bladder was chronically inflamed and contained many stones.

Exploration of the common bile duct showed that the bleeding in each instance was caused by a stone eroding into a blood vessel. In the first case bleeding originated in an ulcerated thin-walled varix; this vessel bled quite actively and was responsible for the profuse hemorrhage into the gastrointestinal tract. Ligation of this vessel was followed by prompt cessation of all bleeding. In the second case the erosion of the ductal mucosa was superficial and the bleeding was trivial. No ligation was necessary here to control bleeding, as it stopped spontaneously when digital pressure was applied to the duct wall at the point of bleeding. In the third case the exact site of the bleeding vessel could not be found because of its distant location, away from the exploratory incision in the choledochal wall. Judging from the profuse hemorrhage which followed removal of the stone in this case, it is judicious to assume that the vessel affected was of a fairly good size. In this instance, as in the first case, bleeding was well controlled after ligation of the vessel in question.

In summary, it may be said that the findings noted in the common bile duct at operation were indicative of ulceration into a blood vessel caused by an eroding stone. Ulceration of the blood vessel was the direct cause of bleeding in every instance, and the amount of bleeding was proportionate to the size and condition of the vessel affected.

The surgical conditions most likely to be confused with choledochal bleeding are duodenal ulcer, gall-bladder disease, or neoplasm of the common bile duct. Radiograms are of great value in diagnosis and should be made in all suspected cases. Duodenal ulceration seldom gives rise to confusion in diagnosis, unless the ulcer is small and situated posteriorly. In such cases visualization will only be possible if oblique films are taken. Duodenal deformity, as distinct from ulceration, not infrequently occurs as a result of surrounding adhesions or pressure by an enlarged gall bladder. Such was the case in our first patient, where dense adhesions surrounding the duodenum caused a deformity of the cap and gave an erroneous impression of duodenal ulcer. The condition may also mimic gall-bladder trouble or carcinoma of the bile duct to a nicety. Maldiagnosis in these cases, however, has no repercussion on the patient, as surgical intervention via the same route is desirable in all cases.

It is quite evident from the foregoing discussion that bleeding from the common bile duct of whatever cause may readily elude diagnosis despite the carrying-out of what is usually regarded to be a complete clinical investigation, even including exploration of the abdominal cavity. This applies with special emphasis to all of our cases. Though there are numerous sources of difficulty which have already been discussed, there are two outstanding reasons for missing the true diagnosis. First, it is not thought of, and, second, sufficiently deter-

mined efforts are not made to obtain a definite picture of this rare complication. It is not unnatural, therefore, when the diagnosis is not made preoperatively. The diagnosis should really present no difficulty once the suspicion of ductal bleeding is raised; it is easy to confirm or disprove the suspected diagnosis at operation.

From the foregoing analysis it would seem safe to postulate that when a surgeon is faced with a patient who presents symptoms such as those described in our series, namely, evidence of blood in the gastrointestinal tract and signs of gall-bladder and common duct disease associated with stone formation, the possibility of ductal bleeding should be seriously entertained. To prove this thesis, one must exclude from diagnostic consideration the presence of a lesion in the alimentary tract and employ all the diagnostic measures in our armamentarium which may help in locating the primary origin of the disease.

Although the present series of cases is small and the problem complex, certain points emerge which may be of value in determining the type of case in which surgery should be given early consideration. A fatal choledochal hemorrhage is rare and, as far as we have been able to determine, previously unsuspected complications of common duct stones and hemorrhage have rarely been observed. It is clear that the majority of these conditions are remediable, and that poor results could be attributed to delay in diagnosis, inadequate preoperative preparation, and sometimes to a failure to realize the real nature of the lesion at operation.

In dealing with the surgical management of choledochal bleeding it is essential to have a comprehensive knowledge of the anatomy of the parts involved, especially as it concerns the vascular supply of the common bile duct. Flint [2] stated that in opening the common duct it is quite common to have an annoying hemorrhage from an artery which crosses the front of the supraduodenal path of this duct. We have investigated the arrangements of the vessels in the common bile duct and found that the main artery to the duct arises from the gastroduodenal artery; it often anastomoses quite freely with a branch of the pancreaticoduodenal artery. Henley [3] made an extensive study of the anatomical distribution of the blood vessels to the bile duct. He noted that the common bile duct receives its blood supply essentially from one artery, which was first described by Wilkie in 1911; it is called the retroduodenal artery of Wilkie. The vessel originates from the gastroduodenal artery and ends by anastomosing, in most instances, with the posterior branch of the inferior pancreaticoduodenal artery. Henley emphasizes the surgical importance of the anatomy of this vessel to the duct, for, where it does not anastomose freely with the inferior pancreaticoduodenal artery, ligation of the vessel proximally may result in gangrene of the terminal part of the duct and a biliary fistula, or may be responsible for the occurrence of a common bile duct stricture some weeks or months after apparently uncomplicated surgery.

The most important problem confronting the surgeon on opening the abdomen is that of making a firm diagnosis which will justify the major steps he is about to take. The gastrointestinal tract should be first investigated along its entirety for a possible bleeding lesion. If none is found, the attention of the surgeon should then be drawn to the biliary tract. The common bile duct should be opened and thoroughly explored. Where the lesion is within view, the question of treatment is very much simplified. If the vessel affected is small and the bleeding can be controlled by digital pressure alone, the mere removal of the eroding stone will suffice, in most instances, to prevent recurrence of the bleeding; such was the case in our second patient. On the other hand, if the vessel is large or cannot be visualized and the bleeding cannot be controlled by digital pressure, then ligation of the vessel becomes imperative. This procedure was employed in two of our cases with excellent results. As already indicated, there is al-

ways the danger of ischemic necrosis of the duct with possible fistulous formation when its arterial supply is shut off, but this is one of the risks which the surgeon must take when he is confronted with such a serious problem as uncontrollable hemorrhage.

Summary

A review is presented of three cases of choledochal hemorrhage secondary to ulceration of a ductal vessel by a stone.

Bleeding from the common bile duct of whatever cause is most uncommon, and that due to stones is exceedingly rare; references to such an event are very scant in the literature.

Some of the problems associated with the etiology, diagnosis, and management of these cases are discussed.

In most instances where bleeding from the duct is trivial, the mere removal of the irritating stone and the application of local pressure is sufficient to control bleeding and prevent recurrence of the hemorrhage. In cases where the involved vessel is of a large size and the bleeding profuse and uncontrollable by local pressure, it may become necessary to ligate the bleeding vessel. Such a procedure is sometimes fraught with danger, as ligation of the artery to the duct is apt to be followed by ischemic necrosis and fistula formation of the common bile duct, especially in cases devoid of adequate collateral circulation.

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Sarcoidosis Associated with Sudden Death During Mitral Valvulotomy

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The manifold signs and symptoms associated with sarcoidosis have in recent years received considerable attention. Originally described as a disease of the skin and lymph nodes, it is now recognized as a systemic disease of unknown etiology which may be localized or widespread in any organ or part of the body.

Sarcoidosis itself as a cause of death is not frequent. It is only when sarcoid involves the heart (primarily, or secondarily following pulmonary fibrosis), the brain, or, possibly, the kidneys, that the uncomplicated disease proves fatal. Death generally is due to some complication.

Perhaps the commonest complication is heart failure secondary to extensive involvement of the lungs producing chronic fibrosis or emphysema.[1]

Since Bernstein,[2] in 1929, first described sarcoid lesions in the heart, attention has been focused on this disease as an infrequent cause of sudden death, by involvement of that organ. In 92 autopsies as reported by Longcope[1] there was involvement of the heart in 20%. Stephen[3] reported a case of sudden death in a 47-year-old white man who at autopsy was found to have extensive myocardial involvement by sarcoid, and Stephen collected eight other cases described in the literature in which sudden death was attributed to myocardial sarcoidosis. All but one of the eight cases were in Negroes.

Scotti,[4] in discussing one case of myocardial sarcoidosis, was inclined to blame the sudden death on involvement of the pacemaker, or bundle of His, causing ventricular fibrillation. This has however, not been proved, but, on the other hand, there have been found minor irregularities and electrocardiographic abnormalities unaccompanied by any untoward symptoms on routine examination. Of 21 patients with sarcoidosis, Leitner found only 8 records that were absolutely normal.[10]

McCort * made electrocardiographic studies in eight cases, and only three of the records were normal. There was right axis deviation in three, left axis deviation in one, and abnormal P waves in one. One patient whose electrocardiogram was typical of right axis deviation died of cardiac failure. The autopsy disclosed extensive sarcoidosis of the lungs, but no lesions were demonstrated in the myocardium. Severer disturbances of transient heart block were observed in one patient, and another with a shifting pacemaker with periods of nodal rhythm has also been described.[1]

Lung lesions in sarcoidosis are common. In 92 autopsy cases of sarcoidosis collected from Johns Hopkins Hospital and the literature, 86% were found to have involvement of the lungs. On the other hand, in 90 cases of sarcoidosis at the Johns Hopkins Hospital, associated lung lesions were diagnosed in only 70% of the cases in vivo, by physical examination and roentgenography. In 25 of the patients physical examination alone did not reveal any pulmonary abnormality.[1]

Submitted for publication Feb. 21, 1956.

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* McCort,[5] cited by Longcope.[1]

On pathological examination there is frequently seen extensive fibrosis of the lungs, associated with the characteristic granulomatous lesions. In some instances fibrosis has been described as the sole residium, with no active lesions present.[7]

The important alteration in the physiology of breathing is an interference with the diffusion of oxygen across the alveolar capillary septa, a condition known as alveolar capillary block. This leads, among other disturbances, to progressive dyspnea and cyanosis and to increase in the pulmonary artery pressure. In addition to the deleterious action that these changes have upon the heart must be added the mechanical interference to the flow of blood through the finer pulmonary vessels, produced by thickening and narrowing of their walls, and development of obliterative endarteritis, as described by Tice and Sweany.[9] The combination of these factors explains the development of cor pulmonale and cardiorespiratory failure in patients with sarcoidosis.

In Rubin and Pinner's [8] collection of 26 fatal cases of sarcoidosis, 8 died of cardiac failure. Pulmonary fibrosis with cor pulmonale was found in seven of these, and sarcoidosis in the heart, in only one.

Report of a Case

A 48-year-old Irish-born omnibus driver was admitted to The New York Hospital on May 13, 1955, complaining of shortness of breath. He stated that so far as he knew he had never had rheumatic fever but that a heart murmur had been discovered 15 years prior to admission. Four and a half years previously he had first noted shortness of breath on climbing stairs. Two and a half years previously, while shoveling snow, he developed marked shortness of breath and mild hemoptysis with cough and orthopnea which persisted for several hours and until a doctor gave him "some shots" which put him to sleep Since this time he estimated he had had 14 such episodes of pulmonary edema brought on by exertion. The last one was 10 weeks prior to admission and was also accompanied by hemoptysis. The patient felt that his exercise tolerance had been gradually but progressively decreasing for the past three years. He had been receiving digitalis for the past seven months, with only very slight improvement. At the time of admission the patient could, with effort, climb six steps, could not lie flat in bed, slept on two pillows, and was able to walk only a half a city block on level ground. There were frequent attacks of nocturnal dyspnea. The patient had lost 25 lb. in the past year. Nine weeks before admission he had fever and chills, diagnosed as pneumonia by his local physician. The patient received no medications and recovered in a couple of days.

Past History.—Hay fever yearly up to 1935, none since. Herniorrhaphy in 1926.

Family History.—Father died at the age of 89; mother died at the age of 85, causes unknown. There is no family history of rheumatic heart disease or fever.

Review of Systems.—Patient has morning cough productive of some grayish sputum. History of peptic ulcer since 1935; no symptoms for the past two years.

Physical Examination.—The patient was a thin, chronically ill-appearing person. There was no cyanosis, but there was moderate clubbing of the fingers. Temperature on admission was 37.5 C. The pulse rate was 84 beats per minute and was regular. Respirations were 12 per minute, and blood pressure was 120/70.

Examination of the chest revealed the heart to be enlarged to the midclavicular line. There was a presystolic thrill at the apex. P_2 was loud, and there was a right ventricular heave. A loud long murmur of mitral stenosis could be heard, but there were no other murmurs. There was a loud M_1 opening snap. Percussion and auscultation of the lungs did not reveal any abnormalities. Palpation and percussion of the abdomen revealed the liver to be enlarged 1 fingerbreadth below the right costal margin and nontender. The spleen was palpable, firm, and nontender 2 fingerbreadths below the left costal margin. The dorsalis pedis pulses were absent. All other peripheral pulses were present, and there was no dependent edema. No peripheral lymph node enlargements were noted.

Laboratory Procedure.—Venous pressure: 140 mm.

Urinalysis: Yellow color, cloudy. Specific gravity 1.07 on one determination. No albumin, sugar, or acetone. Microscopic examination: no red blood cells; 0-2 white blood cells; 5 hyaline casts per high-power field.

Complete blood cell count: RBC, 4,600,000. Hemoglobin, 14.0 gm. WBC, 11,500. Lymphocytes, 14%; monocytes, 4%; eosinophiles, 15%; basophiles, 2%; polymorphonuclear cells, 65%; eosinophile count, 1150 per cu. mm.

Sedimentation rate: 20 mm. in an hour.

Blood chemistry studies: BUN, 13 mg.; blood sugar, 79 mg.; thymol turbidity, 4 units; cephalin

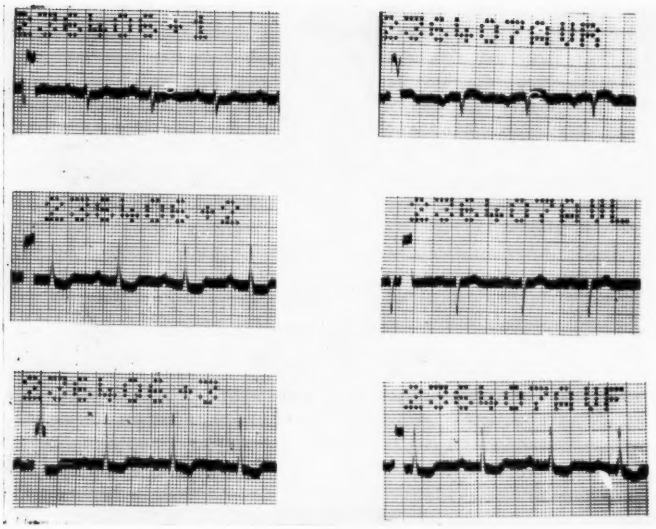

Fig. 1.—Electrocardiogram.

flocculation, 10; protein 6.2 gm.; albumin-globulin ratio, 3.6/2.6 gm.

Stools: negative for ova and parasites.

Electrocardiogram (Fig. 1): Normal sinus rhythm. Right axis deviation. P-R conduction in Lead II, 0.24 seconds; QRS conduction in Lead II, 0.07 seconds. ECG waves: QRS in Lead I, low, split, and varying. Q wave present in Leads II and III. T wave positive in Lead I. T wave diphasic in Leads II and III. R-T interval slightly depressed in Leads I, II, and III. T wave diphasic and coved in Lead V_1. T wave positive in Leads V_2 to V_4. T wave diphasic in Leads V_5, V_8, and V_6. R-T interval slightly elevated in Lead V_1. R-T interval slightly depressed in Leads V_5 and V_6. The right axis deviation is probably due to the vertical position of the heart. The form of the T waves and the R-T segments is abnormal and is probably due to the digitalis effect. The P-R interval is prolonged and may indicate overdigitalization. Marked clockwise rotation is present, suggesting beginning right ventricular hypertrophy.

X-Rays: Chest plate (Fig. 2). The heart is enlarged, with a straight left border, and the barium-filled esophagus is displaced posteriorly in the region of the left atrium. The appearance of the heart is compatible with the clinical diagnosis of rheumatic heart disease with evidence of enlargement of the left atrium and probably left ventricle as well. There is some congestion of the hilar vessels. The remainder of the lung fields are clear. Impression: Rheumatic heart disease with cardiac enlargement as described.

Gastrointestinal series. This showed a deformed duodenal bulb compatible with a healed duodenal ulcer.

Subsequent Course.—It was the concensus of the cardiovascular group that the patient had mitral stenosis, secondary to rheumatic heart disease. There were several disquieting features, however, that were observed and discussed without arriving at a satisfactory explanation. These included hepatosplenomegaly, eosinophilia, and elevated

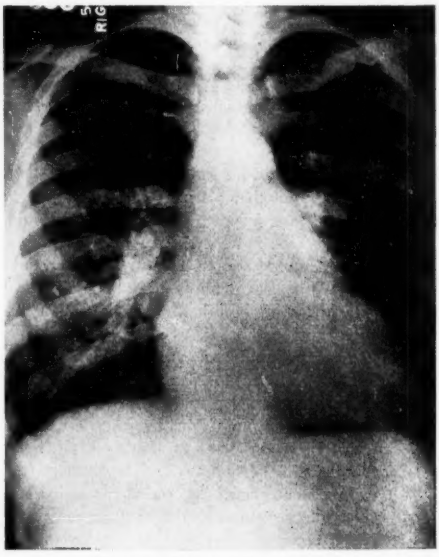

Fig. 2.—Chest roentgenogram.

sedimentation rate. However, after almost two weeks in the hospital no contraindications to operation had been demonstrated in spite of thorough investigation. The patient was desperately in need of correction of his pulmonary hypertension, and mitral valvulotomy was agreed upon. Cardiac catheterization was not performed.

On May 25, 1955, after a premedication of 0.2 mg. of atropine sulfate, the patient was anesthetized with 100 mg. of 2.5% thiopental (Pentothal) sodium intravenously. An endotracheal tube was inserted, and the patient was given ether analgesia. At the time of induction of anesthesia and in the early phases of the operation there was some concern over the patient's status, as he developed cyanosis rather rapidly, and he was, therefore, kept in a very light plane.

Operation: The left chest was slightly elevated on the table. An incision was made from the left second rib at the sternal border, curving below the breast into the axilla. There was moderate cyanosis in the superficial venous circulation at this time. The fourth rib was resected subperiosteally, and the pleura was opened. There was only minimal fluid in the pleural cavity. The lung was allowed to remain expanded in order to maintain oxygenation. The pericardial sac was full, and the heart was slightly enlarged to the left. The pericardium was somewhat edematous. Beneath the pleura, at the arch of the aorta, there were two lymph nodes measuring 5×1.5 cm., dark brown in color, not unlike those seen in Hodgkin's disease. One of these was removed.

The pericardium was incised anterior to the phrenic nerve. The pulmonary artery, which was enlarged to about four times normal size, was very tense. The auricular appendage was enlarged, and the coronary arteries were tortuous. Manipulation of the heart appeared to cause little in the way of stimulation. There was no fall in blood pressure. Pressure was maintained on the carotids as the auricular appendage was palpated. No thrombus was felt.

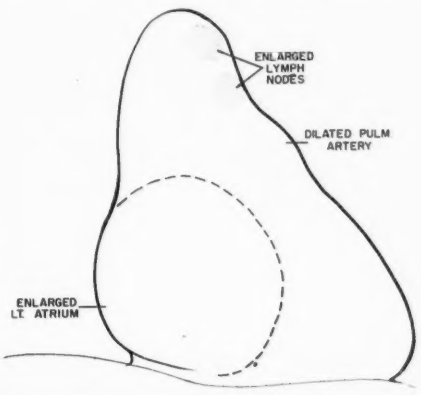

Fig. 3.—Schematic drawing of operative findings.

The base of the appendage was now infiltrated with 1% procaine hydrochloride, and pursestring braided nonabsorbable surgical (silk) sutures were placed. A Statinsky clamp was placed on the auricular appendage, and the tip was excised, dividing also the trabeculae. The inside of the auricle was bright and glistening, with no evidence of clot formation. Stay sutures were now placed on the cut margin; the clamps were removed, and the index finger was inserted into the auricular appendage. The auricle was rather large, and there was no regurgitation. There was marked stenosis, and the mitral orifice was estimated at less than 1 sq. cm. There was a definite bulge of the anterior leaflet and some calcium deep in the valve medially and posteriorly. Separation of the commissures was now acomplished both medially and laterally, enlarging the orifice to about 3-4 sq. cm. Up to this time there had been little disturbance of the electrocardiogram. As the finger was being withdrawn from the heart, the pulse began to slow. The pursestring sutures were tied, and while this was being done complete standstill occurred. At the same time it was observed that there was complete cessation of activity both on the electrocardiogram and the electroencephalogram. Cardiac massage was instituted immediately and continued for 1 hour and 10 minutes. The patient received calcium chloride, ephedrine, isoproterenol (Isuprel), and atropine, but to no avail. At no time during this period was there any evidence of fibrillation. The pulse had been slow and just became slower and then stopped. All resuscitative measures were ineffective. There was a complete lack of any activity as far as cardiac action was concerned after the arrest had occurred.

Postmortem Examination.—Autopsy was performed two hours after death. The findings were as follows: Rheumatic heart disease with mitral stenosis and hypertrophy of the heart. The heart weighed 520 gm. Both ventricles, particularly the right, were hypertrophied. Their walls measured 15 and 6 mm., respectively, in thickness. The right and left auricles were dilated. The leaflets of the mitral valve were greatly thickened, and chordae tendinae formed a fused mass with the papillary muscles. A thick fibrous band bound the two papillary muscles together. The circumference of the valve at the base of the leaflets was 9 cm. The lateral commissure was split for a distance of 2 cm., but there was only minimal separation medially. In addition to hypertrophy of myocardial fibers and diffuse and focal fibrous replacement of myocardial fibers, a few typical Aschoff bodies were found in the interventricular

Fig. 4.—Fibrosis and arteriolar sclerosis of lung; reduced from mag. × 40.

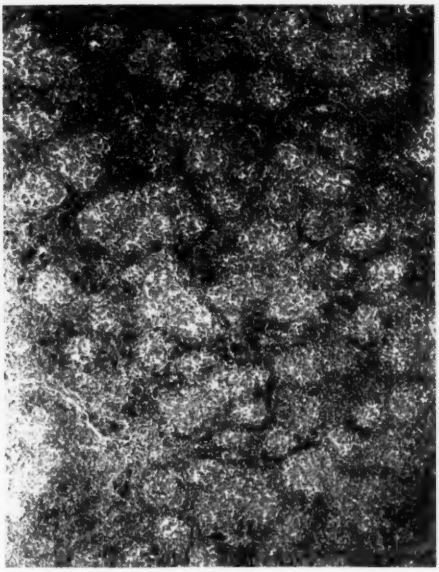

Fig. 5.—Sarcoid lesions in mediastinal lymph node; reduced from mag. × 40.

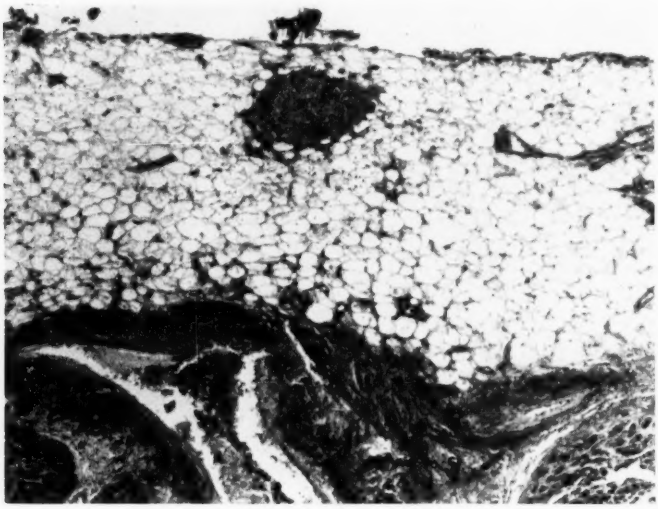

Fig. 6.—Sarcoid granuloma in left auricular wall; reduced from mag. × 67.

septum and posterior wall of the left ventricle. Many subendocardial small rheumatic-type granulomata were found in the left auricualr appendage.

There was chronic passive hyperemia of the lungs, liver, and spleen. The lungs weighed 1660 gm. together. The lobes were moderately firm, and the cut surfaces were hyperemic. The liver weighed 1810 gm. and was hyperemic. The spleen weighed 400 gm. The deep cervical, mediastinal, and bronchial lymph nodes were markedly enlarged, some measuring up to 3 cm. in diameter. They were soft and discrete. The cut surface was hyperemic and contained numerous prominent gray nodules.

Microscopic sections revealed numerous small noncaseous granulomata containing multinucleated

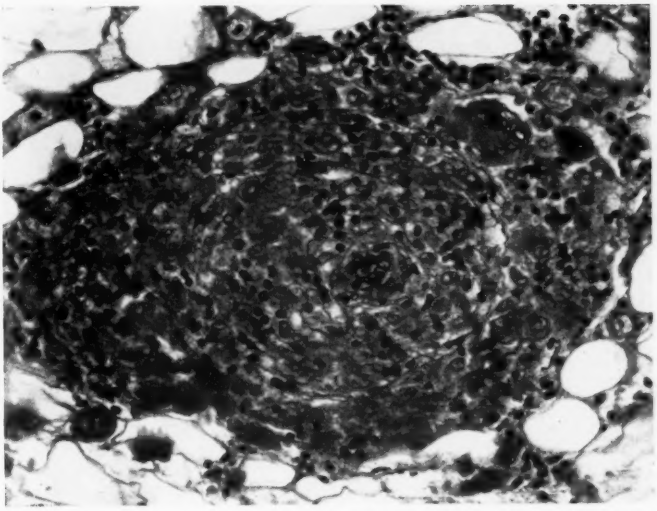

Fig. 7.—Sarcoid granuloma in left auricular wall; reduced from mag. × 365.

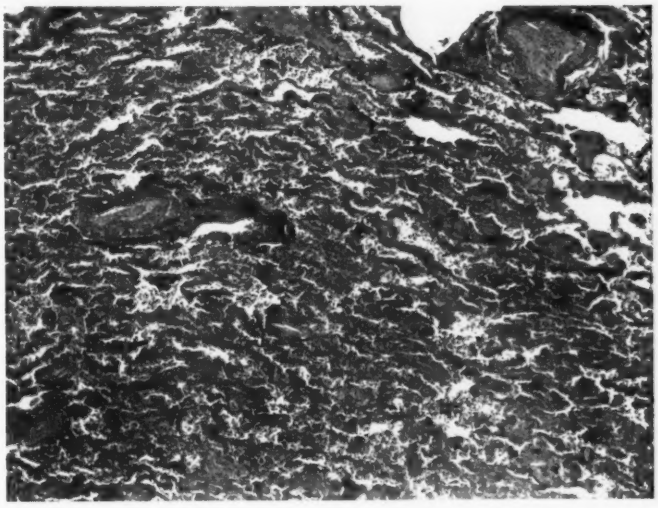

Fig. 8.—Fibrosis and arteriolar sclerosis of lung; reduced from mag. × 40.

giant cells in mediastinal (Fig. 5) and pancreatic lymph nodes, and there were occasional such granulomata in the myocardium and epicardium (Figs. 6 and 7). These were typical of sarcoid lesions. The lung parenchyma showed marked fibrosis and arteriolar sclerosis (Fig. 4). The brain was grossly normal on sectioning.

Comment

The actual mechanism of death in this case is not clear. The diagnosis of sarcoidosis was not made preoperatively, although the patient was studied carefully in the hospital. The sarcoid lesions in the heart were hardly extensive enough to cause acute myocardial failure, and disturbances of conduction or ventricular fibrillation did not occur. Death occurred by slowing and then standstill of the heart, which was exposed in the operative field, and simultaneous disappearance of activity on the electrocardiogram and electroencephalogram, after the

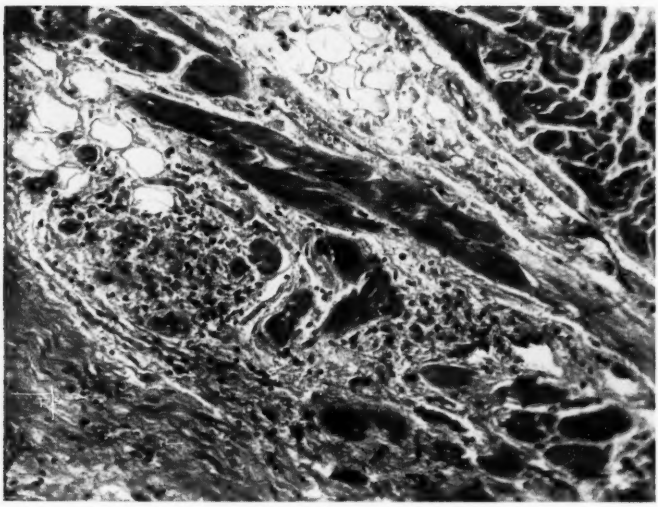

Fig. 9.—Sarcoid granuloma in interventricular septum; reduced from mag. × 180.

crucial point in the operation had been accomplished, i. e., the separation of the leaflets of the mitral valve, when successful outcome was to be expected. The simultaneous cessation of heart and brain activity suggests some factor involving both organs at the same time, one independent of the other. In uncomplicated mitral stenosis the barrier is at the stenotic valve, and, in spite of the pulmonary fibrosis secondary to the back pressure of blood, relief is usually marked and immediate following successful commissurotomy. In this patient the fibrosis and arteriosclerosis of the lungs was much more marked than in the ordinary case of advanced mitral stenosis, caused, we think, by healed lesions of the sarcoidosis in the lung parenchyma, as described by Ustvedt.[7] As we know that cardiac failure secondary to pulmonary fibrosis of sarcoidosis can cause death, it might be suggested that the important barrier to blood flow and oxygenation in this case was primarily in the lungs. Accordingly, the important benefit from the commissurotomy did not take place, as the mitral stenosis was a secondary obstacle and its correction did not change the primary problem. Accordingly, the unfulfilled additional demand of brain and heart tissue for oxygenation during the operation may have reached the critical point at which death occurs.

Summary

A case of mitral stenosis with associated sarcoidosis is presented. It is suggested that involvement of the lung parenchyma played a decisive role in causing this patient's death during mitral commissurotomy.

Conclusions

In spite of normal chest roentgenograms, thorough pulmonary-function studies should be carried out prior to mitral commissurotomy in patients with known sarcoidosis, as extensive pulmonary fibrosis from the healed sarcoid lesions may prevent an otherwise successful outcome.

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Healing of Anorectal Wounds with Reference to "Rectal Medication"

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Under the impact of modern chemotherapy it became abundantly clear that potent therapeutic agents, such as the steroid hormones, when applied to the anogenital area in a vanishing type base (cream) exert a profound local pharmacologic effect, e. g., in pruritus. In numerous instances, when these same drugs are applied in an oleagenous ointment or grease base they are ineffective, and vice versa. These observations as well as subsequent studies led to our almost complete discontinuance of the topical application to the anogenital skin of drugs in oleagenous ointment, a vehicle which one of us had employed in the past.* In line with the foregoing and other observations, we instituted an investigation of the effects of various therapeutic agents in ointments and creams on the healing process of the anorectal wounds; to some of these agents healing-promoting qualities had been attributed by authors or in the promotion of marketed preparations.

Method and Procedure

After the performance of the open technique of hemorrhoidectomy[3] (Fig. 1.), the anorectal wounds of alternate groups of 15 patients were treated with the following medications: (*a*) an ointment containing cod liver oil[2]; (*b*) an ointment containing vitamins A and D; (*c*) hydrous wool fat U. S. P. (lanolin); (*d*) a hydrophilic cream containing chlorophyll; (e) hydrophilic cream containing hydroxyquinoline; (*f*) hydrophilic ointment U. S. P., and (*g*) a bland lubricating mixture of water-soluble gums or tragacanth paste. The wounds of 10 additional patients were treated with an ointment containing 2% ethyl aminobenzoate (Benzocaine) among other ingredients. These medicaments were applied to the wounds by means of a gloved index or little finger every two to three days beginning on the fifth postoperative day, until complete healing of the wound took place. This maneuver was a part of the postoperative management to promote healing or granulation from the bottom out and to prevent or to break up any bridging of the skin. Hydrous wool fat, hydrophilic ointment, lubricating jelly, or the tragacanth paste was intended as a control, but as the results began to reveal themselves during the course of this clinical experiment it was decided to reinforce this control by an "ultracontrol." For this purpose 10 patients were accorded only one digital rectal examination (using bland lubricating jelly) on the seventh postoperative day to make sure of the immediate integrity of the wounds and another digital examination was done after apparent complete healing of the wounds.

As the clinical results described elsewhere in the text began to reveal themselves, contemplated animal experimentation such as that described by Dann and associates[4] was abandoned at least for the present. This change of plan was also partially motivated by the knowledge that the results of animal experimentation cannot always be translated or carried over into human biology or human experience. Furthermore, we were not sure that experimentally produced wounds in the anorectum of a quadruped animal compare with those produced by removing pathologic tissue from human rectums.

As this investigation progressed, alternate groups of 10 patients were subjected to plans (*a*), (*b*), (*c*), (*d*) and (*g*) after excision of anal ulcers and the performance of either classic or modified posterior sphincterotomies by the technique already

Submitted for publication Jan. 6, 1956.

* References 1 and 2.

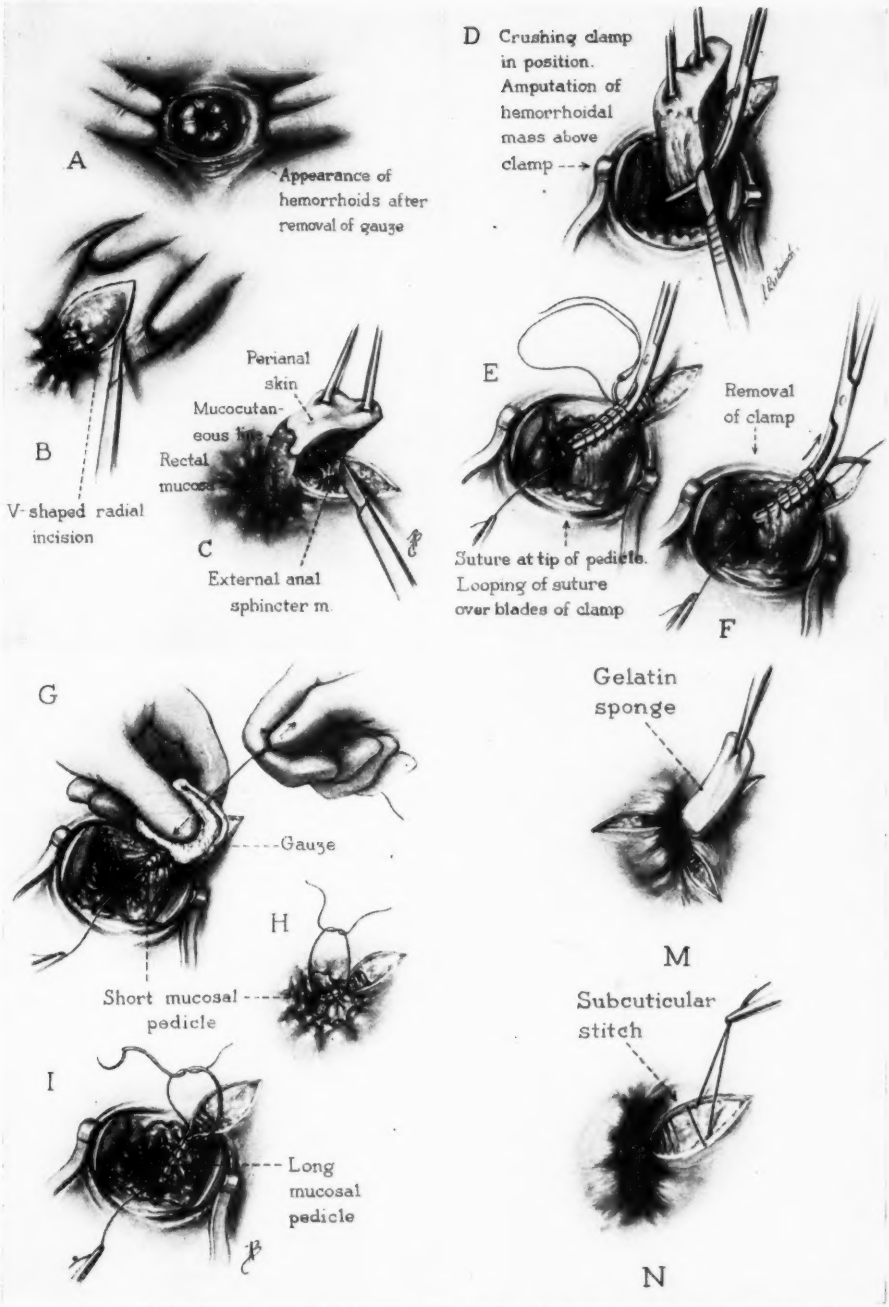

Fig. 1.—Technique of hemorrhoidectomy employed in this study. Note the sphincter identified as the "external anal sphincter muscle" in C has, according to the most recent anatomic studies, been shown to be the lower margin of the internal sphincter muscle (from Turell, R.: *S. Clin. North America* 32:677 [April] 1952, published by W. B. Saunders Company, Philadelphia).

described[5] (Fig. 2.). Five patients were utilized as "ultracontrols."

Clinical Results

The hemorrhoidectomy wounds (controls included) in all groups, except for three of those patients who received an anesthetic, healed uneventfully within about 21 to 25 days. The anoperineal skin of the three patients who received anesthetic drugs was the site of edema, reddening, and pruritus, this reaction being intense in one instance, after about two to four applications, necessitating the prompt discontinuance of the medication. Excessive granulation tissue requiring one or two applications of silver nitrate occurred in the wounds of over 10% in all groups. These results parallelled the pattern of healing that was observed in personal experience with over 1,000 open type hemorrhoidectomies; seldom did complete healing take place in less than three weeks.[6] Complete and uneventful healing without recurrence was observed within one month after excision of anal fissures, also conforming to past experience.[5]

Reliance was placed on these purely clinical observations, even though it is realized that these do not necessarily compare in all respects with the absolute scientific proof or evidence obtained from animal experimentation.

Comment

The startling finding in the present investigation was the fact that all wounds, except for three in the group that received an anesthetic ointment, healed, uneventfully with equal rapidity and completeness. Neither during the postoperative period nor after completion of healing of the wounds could one discern the slightest difference either in the rate of the healing process or in the quality of the resultant scars. As already noted, these results followed the usual pattern of healing observed long ago.† Failure of the medicaments employed in this study to expedite the healing process confirms the well-known biological fact that the healing process of surgical wounds anywhere in the body may be delayed but cannot be expedited[7] because under normal conditions the natural healing process proceeds at a maximum rate.

For the sake of emphasis it is reiterated that by the techniques of hemorrhoidectomy and fissurectomy with sphincterotomy employed in this study only the pathologic tissue is removed; mass clamping and bulk ligation are avoided, and the normal anal integument between the wounds is preserved (Figs. 1, 2.). These operations are followed by an extremely low incidence of complications. Of historic interest is the fact that the underlying principles of the type of hemorrhoidectomy employed here had been enunciated and practiced by Hippocrates.

The most unexpected fact that emerged from this clinical study was that the wounds of the "ultracontrols" healed just as effectively and rapidly as did those in patients who received the medication and the conventional postoperative anal digital explorations. This observation suggests that uneventful healing of wounds depends more on the type of surgical procedure performed and on the gentleness in handling tissues during operation than on either the postoperative topical application of therapeutic agents to the wounds or the performance of periodic anal digital explorations. This is contrary to established proctologic teaching, custom, habit, and tradition; the passage of the lubricating finger into the anal canal appears to be routine practice with most, if not all, proctologists. Some proctologic surgeons even train their patients how to carry out this digital maneuver themselves and instruct them to pass their index fingers once or twice daily for about a month after discharge from the hospital. A few other proctologic surgeons instruct their patients in the use of dilators which are inserted daily or every other day into the rectums by the patients. On the basis of the observations in military (when one of us had

† References 3 and 5.

Fig. 2.—Technique of fissurectomy and sphincterotomy employed in this study. Note the herein illustrated subcutaneous sphincter muscle, which is a part of the external anal sphincter, has, according to the most recent anatomic studies, been shown to the rounded lower margin of the internal sphincter (from Turell, R.: *Surg. Gynec. & Obst.* 86:434 (April) 1948, published by the Franklin H. Martin Memorial Foundation, Chicago).

a chance to observe the end-results of proctologic operations performed by surgeons of many parts of the United States) and civilian practice, both private and clinic, it appears that the excessive and pernicious use of the rectal dilators or the index finger by the surgeon or patient is dictated by the dire need resulting from a poorly conceived technique or a poorly executed initial orthodox operation. In these instances, too much normal anal integument is needlessly sacrificed or insufficient elastic anal skin between wounds is preserved. The performance of such procedures, even though it may be favored by some proctologists, particularly by those who perform the so-called "plastic" or other high-sounding techniques may prove a trap for the unwary or younger surgeon.

After eventual healing of such wounds the resultant scar tissue is resistant and hence lacks the elasticity or expansion that is essential to normal defecatory effort. This may lead to or terminate in anal dysfunction or even narrowing requiring incision of scar tissue postoperatively in many cases (13% is a figure stated in a most recent report). In our experience, postoperative anal stenosis has usually failed to respond to dilations or mere radial incisions into the scarred tissue; a formal corrective operative procedure is invariably required.[8] It should be borne in mind that scar tissue, no matter how thin or flat, is abnormal tissue—it is no substitute for or replacement of elastic skin, particularly in the older age group of patients. The frequency of occurrence of such postoperative inadequacies or failures, let alone outright stenosis, mars the glorious record of modern proctologic surgery—a field that is of special interest to many general surgeons.

The occurrence of effective healing of anorectal wounds without the aid of medicaments as noted in this study speaks against the need for these and/or other medicaments, including the steroid hormones,[9] which may be used by some proctologists allegedly with a view to enhancing the healing process or to preventing irritation or to combating infection to which anorectal wounds are said to be particularly vulnerable. The fallacy of the last statement lies in the well-known fact that mild or minimal infection of wounds is harmless because the normal healthy tissue cells are not only endowed with competent defense mechanisms but their vigor may be stimulated by a mild infection. This is particularly true of the tissues in the anorectum, which are provided by a special environmental immunity to infection and an extremely abundant blood supply and nerve network. These tissues do not require the help of the therapeutic agents mentioned herein or of any antiseptic drugs, which in a broad sense are biologic cellular poisons and hence may be harmful. On the other hand, the anogenital skin, in common with the skin of the remainder of the body, may be sensitive to the derivatives of the cocaine group of drugs. As already stated, 3 of the 10 patients who received ethyl aminobenzoate ointment showed cutaneous sensitivity even though the release of drugs from ointments is limited. The same drug applied in a vanishing-cream base might have wreaked havoc in these three patients as evidenced by patch tests which revealed similar sensitivity to these drugs in other parts of the body. The seriousness of cutaneous sensitization by this group of drugs has been well appreciated and commented upon by dermatologists.‡ The lack of general appreciation of these facts is partially explained by what Goethe once said: "What one knows, one sees."

Clinical Application

It is apparent from this limited study that anorectal wounds are capable of healing uneventfully without frequent anal explorations, digital or instrumental. The passage of normally formed stool daily or every other day conceivably breaks up superficial bridging or adhesions and facilitates granulation to proceed from the bottom out. Many

‡ References 10 and 11.

intestinal surgeons § hardly ever perform more than two or three digital explorations after hemorrhoidectomy or fissurectomy. As already stated, the type of operative procedure employed and the gentleness in handling tissue during operation appear to be of prime importance.

While there is no undue objection to a greater frequency of performance of digital explorations by the surgeon, it is decidedly unwise to perform these procedures daily, or to entrust to the patient the passage of a finger or dilators into the rectum. Besides the potential physical harm, digital or instrumental manipulation of the anal region, which is an erogenous zone, carries the oft overlooked but important psychosexual problem or danger. In some patients, this practice serves as a form of sexual gratification and establishes a perverted habit that is difficult to break.[12]

As already stated, the topical application of either cod liver oil or of vitamins A and D in oleagenous ointment bases to surgical anorectal wounds in no wise appears to be superior to nonspecific substances such as hydrous wool fat U.S.P., hydrophilic ointment U.S.P., or a jelly made up of water-soluble gums. These findings are contrary to a former impression that one of us gained from a clinical study without employing adequate controls.[2] At the time of that study he was interested neither in establishing nor in enhancing the rate of healing. It was then stated that "in the absence of controls, no attempt was made to ascertain the effects of this ointment on the rate of healing of the postoperative anorectal wounds." Mindful of the local deleterious effects of the anesthetic drugs, he was then primarily interested in the procurement of a bland ointment as a lubricant for postoperative anal explorations as a safe substitute for the then prevalently used anesthetic ointments. The clinical observations herein reported are in conflict with Lenson's conclusions: The validity of his experimental controls is decidely open to question.[13] The same criticism justifiably applies to Marks' findings.[14]

Ointments containing cod liver oil or vitamins A and D are bland and are still useful in some forms of dermatitis. However, in common with that of other oleagenous ointments, their employment is objectionable to many adult patients because these ointments are too greasy and hence messy; vanishing creams are preferred. The introduction of petrolatum or ointments containing petrolatum is known to have caused paraffinomas in the anorectal wounds.[15] We encountered such an oleogranuloma recently. The popularity of topical use of the vitamins is the result of empiricism and custom; the last status report on these agents by the Council on Pharmacy and Chemistry appeared as far back as in 1943. Although empiric treatment has had a place in medicine, the referee of the Council rightfully insists on adequate controls.‖ The existing false impression that vitamin A is absorbed through the intact human skin [16] appears to be the indirect result of translating findings from the experimental rat into human biology or medicine.

Chlorophyll also failed to influence the rate of healing of anorectal wounds. Thimann,[17] the Harvard biologist, pointed out that "the material sold as chlorophyll is not chlorophyll at all and does not even merit the name of chlorophyllin" and that "the word chlorophyll, or even chlorophyllin, gives a false impression to the public." He offered to withdraw these and other statements in the face of convincing evidence that it has, among other therapeutic claims, "any greater effect in promoting the growth of granulation tissue in wounds than do a vast variety of other nonspecific materials." The results of the present study lend support to Thimann's frank statement, and we agree with him that "the public is being subjected to a racket of tremendous propor-

§ Ginzburg, L.; Lyons, A. S.; Lesnick, G. J., and Maynard, A. de L.: Personal communications to the authors.

‖ Stormont, R. T.: Personal communication to R. T., Dec. 23, 1952.

tions . . ." Imagination has a place in clinical medicine but must give way to proved facts.

Oxyquinolines (chlorquinaldol [Sterosan]) are likewise devoid of any special qualities pertaining to the healing of anorectal wounds.

In ointment form, anesthetics do not appear to influence the healing of postoperative anorectal wounds. In our experience some 10% to 30% of patients develop cutaneous reactions when derivatives of cocaine, though extremely useful for control of pain, are applied topically to the anogenital area. Because of this high incidence of cutaneous reactions that follow the topical, sometimes promiscuous, application of these drugs or the use of suppositories containing anesthetic agents,[11] we have abandoned their use. Parenthetically, this also applies to the injection of the long-lasting, water- or oil-soluble anesthetic drugs for the control of postoperative pain; a therapeutic crutch that fosters a false sense of security and dependence on a drug that is an extremely poor substitute for good and gentle surgery. This is an example of what Shakespeare probably meant by "Virtue itself turns to vice when misapplied."

Summary

The topical application of cod liver oil, vitamins A and D, chlorophyll, hydroxiquinoline, and ethyl aminobenzoate failed to expedite the healing of anorectal wounds, showing that these agents apparently lack alleged healing or tissue-growth-promoting qualities. These substances were in no wise superior to the controls, which consisted of hydrophilic ointment U.S.P., hydrous wool fat, or water-soluble gums.

Cutaneous sensitivity reactions occurred in 3 of the 10 patients in whom anesthetic drugs were used. Either the water-soluble gums or a hydrophilic (vanishing) cream are good lubricants; oleagenous ointments are too greasy and messy, hence objectionable to many patients.

The most startling and unexpected finding that emerged from this clinical investigation was the fact that the ultracontrols, in whom the postoperative wounds were left practically undisturbed, healed just as effectively as those that received the conventional periodic digital explorations or examinations and special topical medications.

The results of this study confirm and echo the conviction of many general and proctologic surgeons of accomplishment and repute that experience, refinements of technique, gentleness in handling of tissues during operation, and the preservation of sufficient elastic integument between wounds determine the good end-results of anorectal operations. The well-trained and experienced surgeon knows from accumulated established facts that when any one or a combination of these principles is ignored, especially when too much anal skin is unnecessarily sacrificed, poor or disastrous results usually follow that require corrective surgical intervention, as these usually cannot be corrected by anal dilations, digital or instrumental. The present study also lends support to the belief that these anal cripples cannot be helped by topical medications which at best act as therapeutic crutches fostering a false sense of security. Dependence on dilations and drugs is no substitute for basic concepts and sound surgical principles.

25 E. 83rd St. (28).

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Referred Pain from Low Back Ligament Disability

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The purpose of this article is to present substantiated observations on referred pain that will assist physicians in determining the cause of low back pain and disability.

Referred pain areas (Fig. 2) in the lower abdomen, groin, genitalia, buttock, and extremities to as far as the toes have been identified as having their origin in the ligaments that stabilize the lumbar and pelvic articulations.

Ligament relaxation is a chronic disability that results from strain, sprain, and tearing of the ligament fibers when they do not regain their normal tension.

The pain associated with ligament relaxation is induced by stretching of the ligament fibers under normal tension, which permits an abnormal stimulation of the sensory nerves within the ligament, which will not stretch. The abundant supply of sensory nerves at the junction of ligament to bone has been established by Leriche and Gardner.

The method employed to identify the local pain and the referred pain is needling. It consists in inserting the point of a hypodermic needle within the fibrous strands of a specific ligament and the injection of a local anesthetic solution. The irritation of the needle and the pressure of the anesthetic solution will immediately reproduce the local pain, as in dentistry, and frequently the referred pain, only to disappear within two minutes as anesthesia takes place.

In a period of 17 years while giving over 6000 intraligamentous injections, during the confirmation of the diagnosis and treatment of 1017 cases of ligament relaxation, I have found relaxed joint ligaments to be the cause of more chronic low back disability than any other entity and the cause of more referred pain into the lower extremities than all other causes combined.

From observations during the earlier years, the trigger points of ligament pain and the areas of referred pain were included in medical journals and in my book on ligaments, which is the only treatise ever written on ligaments.

Since submitting the manuscript for publication, additional observations have made it possible to design a more comprehensive dermatome of referred pain (Fig. 2) and an illustration of the trigger points of ligament pain (Fig. 1), from which the referred pain originates in the sensory nerves.

History of Referred Pain

Sir Henry Head first used the term referred pain, in 1893. It was my good fortune to have served him as house physician in The London Hospital in 1916.

Lennander reported the origin of pain and referred pain from traction on nerves in the pedicles of abdominal organs.

Baer, with whom I visited European medical clinics in 1925, had reported in 1917 that sacroiliac referred pain passed "down the outer aspect of the thigh" and "sciatic pain to the heel." Neither he nor any later investigators have specifically placed the origin of low back pain and referred pain in ligaments, although a few have included ligaments when naming all the tissues in an area to be infiltrated with an anesthetic solution for the relief of pain.

Many investigators of referred pain have worked from the area of reference, through the spinal posterior root ganglion, in en-

Submitted for publication June 4, 1956.
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deavoring to establish the point of origin of nerve receptor stimulation in an organ or somatic structure, which had its innervation from the same spinal posterior segment.

For the relief of referred pain, much effort has been expended by others in endeavoring to interrupt the pathway of impulse.

Our approach in locating specific areas of referred pain has been direct, by stimulating the reproduction of local pain and its associated referred pain at their point of origin in the ligament and its fibro-osseous attachment to bone, followed by anesthetizing the point of origin to abolish the local and referred pain.

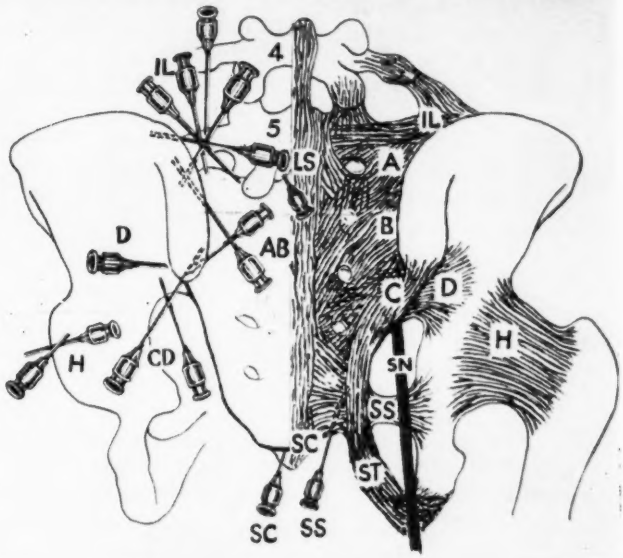
Knowledge of the source of pain is essential for satisfactory diagnosis and treatment.

Perception of Pain and Referred Pain

The ligament fibers crisscross in various directions between articulating bones to maintain stability in all positions and limit motion in all directions.

According to Brain, the normal function of the sensory nerves surrounding the ar-

TRIGGER POINTS OF PAIN AND NEEDLES IN POSITION FOR CONFIRMATION OF THE DIAGNOSIS AND FOR TREATMENT OF LIGAMENT RELAXATION OF THE LUMBOSACRAL AND PELVIC JOINTS.



TRIGGER POINTS OF LIGAMENTS

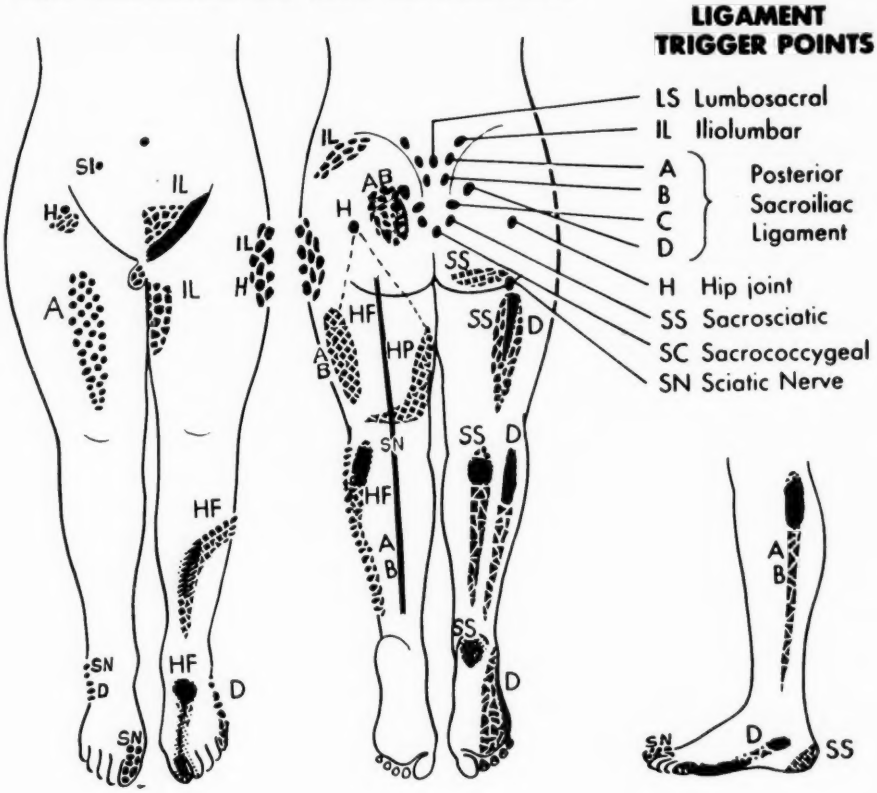
IL - Iliolumbar
LS - Lumbosacral - Supra & Interspinus
A,B,C,D, - Posterior Sacroiliac
SS - Sacrospinus
ST - Sacrotuberus
SC - Sacrococcygeal
H -. Hip - Articular
SN - Sciatic nerve

Figure 1

DERMATOMES OF REFERRED PAIN

by George S. Hackett M.D.

FROM LUMBOSACRAL AND PELVIC JOINT LIGAMENTS



Referred Pain Areas in the Abdomen, Groin, Genitalia, Buttock and Extremities from Relaxation of the Posterior Ligaments which support the Lumbosacral and Pelvic Joints.

IL Iliolumbar ligament (Iliac attachment) Abdomen, Groin, Genitalia, Buttock, Thigh (inner anterior)

AB Posterior Sacroiliac ligament (upper 2/3rds) Buttock, Thigh, Leg (outer surface)

D Posterior Sacroiliac ligament (lower outer fibers) Thigh, Leg (outer calf), Foot (outer margin and sole to 5-4-3-2 toes accompanied by sciatica, loss of ankle reflex and body list)

HP Hip articular ligament (Posterior superior fibers, Pelvic attachment) Thigh (Posterior Medial)

HF Hip, articular ligament (Posterior superior fibers, Femoral attachment) Thigh, Upper half of leg (lateral to calf), Lower half of leg (anterior to tibia), Top of foot to big toe and half of 2nd toe.

SS Sacrospinus and Sacrotuberus ligament (Sacral attachment) Thigh, Central calf of leg, Heel.

SN "Sciatica"- nerve pain accompanying relaxed ligaments (lower end of Sacroiliac joint).

Figure 2

ticular surfaces is propioceptive sensability appreciation of posture on movement of the body.

The afferent impulses from the ligaments enter the spinal posterior root ganglion and are chiefly concerned in reflex activity at the spinal level, or influence the cerebellum in its control of movement and posture. There are related afferent and efferent impulses of the muscles and tendons.

Many of the sensory impulses do not reach consciousness unless there is excessive tension on the ligament, which intensifies the sensory stimulation. Voluntary relief of ligament tension is then accomplished.

When the ligament fibers become relaxed, a normal tension will then produce a bombardment of afferent somatic propioceptive sensory impulses from the ligament into the spinal posterior root ganglion, where some are transmitted to the brain as consciousness of local pain, while other impulses in some way stimulate exteroceptive impulses which also enter consciousness as superficial pain from an area which has its sensory distribution from the same spinal segment and is known as the referred pain area.

I shall not discuss the many theories that have been suggested to explain referred area pain, nor other disabilities of the back about which so much has been written. Neither shall I discuss prolotherapy for joint ligament relaxation, which consists in stimulating the production of new bone and fibrous tissue cells to strengthen the "weld" at the fibro-osseous junction of ligament to bone. It has been successfully developed over a period of 18 years to reestablish the tensile strength of ligaments.

Lumbosacral Joint Referred Pain

Referred pain that is indicative of lumbosacral joint disability has its origin in the attachment of the outer fibers of the iliolumbar ligament to the ilium (Fig. 1, *IL*). The referred pain area in the groin (Fig. 2, *IL*) is the commonest. Other areas are in the anteromedial thigh, the lower abdominal wall, and an aching testicle of the male, and in the female it occurs in the labia minora and extends 2 in. into the vagina on the affected side.

Sacroiliac Joint Referred Pain

Sources of referred pain that is indicative of instability of the sacroiliac joint are as follows: Above, the upper portion of the posterior sacroiliac ligament (Fig. 1, *AB*) has associated referred pain areas in the buttock, the posterolateral thigh, and the outer surface of the leg (Fig. 2, *AB*). The buttock area is almost always present. A burning sensation occurs frequently over the upper end of the fibula and the pain may be referred to within 2 in. of the external malleolus.

Below, the referred pain has its origin in the lower outer fibers of the posterior sacroiliac ligament (Fig. 1, *D*), where they are attached to the outer surface of the ilium beneath the gluteus muscle and just above the sciatic foramen.

Another source of referred pain is from the attachment of the sacrospinous ligament to the outer margin of the sacrum above the sacrococcygeal joint (Fig. 1, *SS*). Superimposed on its attachment are the long posterior sacroiliac ligament and the sacrotuberous ligament (Fig. 1, *ST*).

The referred pain areas from the lower outer posterior sacroiliac ligament attachment at trigger point *D* (Fig. 1, *D*) extend down the posterolateral thigh (Fig. 2, *D*), down the outer margin of the calf of the leg, occasionally beneath the external malleolus as a burning sensation, and more often as a numbness on the outer side of the foot and the fifth toe. Sometimes there is a numbness in the sole of the foot proximal to and extending into the fifth, fourth, third, and second toes (Fig. 2, *D*).

Relaxation of the lower outer posterior sacroiliac ligament at Figure 1, *D* is often complicated by a sciatica, in which the sciatic nerve is painful on traction and tender on pressure (Fig. 1, *SN*) and has its own pains of reference (Fig. 2, *SN*) into the thigh, leg,

and foot, often to the great toe, which complicates the diagnosis. The Achilles reflex may be diminished or absent, as well as the knee reflex less frequently. The calf of the leg may lose up to 1 in. in circumference. There may be a body list and pain of such intensity that morphine will not relieve it, and the patient is unable to lie flat or straight in bed.

To account for the sciatica, I believe that with an intensely irritable ligament, there is an accompanying spasticity and inflammation of the adjoining piriformis muscle which extends into and involves the sciatic nerve as it emerges from the pelvis.

Strengthening of the ligament by fibro-osseous proliferation permanently clears up the local pain, the referred pain, and the sciatica.

Referred pain from the sacrospinous ligament attachment to the sacrum (Fig. 1, *SS*) extends transversely along the lower margin of the buttock, down the posterior thigh, a vertical distribution through the central portion of the calf of the leg, and beneath the heel (Fig. 2, SS). It is most intense at the top of the calf in an area about 2 in. in diameter and when walking may feel like a "hot coal" or "bare bone" beneath the heel. The heel may also be tender on pressure from side to side between the thumb and finger.

After sitting for a while the patient is unable to stand upright or walk until after standing bent forward for a few minutes to relieve muscle spasm.

Referred Pain From Hip Instability

There are two sources of pain from relaxation of the posterior superior fibers of the capsular ligament of the hip (Fig. 1, *H*), and each end of the ligament has a separate area of referred pain.

From the pelvic attachment of the ligament, the referred pain area (Fig. 2, *HP*—hip, pelvis) extends down the posteromedial surface of the thigh and across the popliteal space just above the articular surface of the knee.

The referred pain area from the femoral attachment is located on the posterolateral thigh (Fig. 2, *HF*—hip, femur), the outer margin of the calf in the upper half of the leg, from where it passes around the outer side of the leg to extend down the front of the lower half of the leg. It next appears as a burning sensation on the top of the foot (instep) and extends into the top of the great toe.

Statistics

A survey of 146 consecutive cases of undiagnosed low back disability over a two-month period in 1955, with a distribution from the Atlantic to Pacific and Gulf states, revealed that 94% had joint ligament relaxation with referred pain. The average duration of disability was 10 years. One had submitted to four spinal operations.

A survey of 67 consecutive cases of undiagnosed low back disability from the state of Michigan which were examined in the past two months revealed that 97% had joint ligament relaxation with referred pain. One had submitted to three spinal operations.

The physician who understands ligament disability and the associated referred pain, as well as the associated anatomical components, will be able to diagnose back disability with confidence.

Comment

The presence of referred pain one month after treatment by prolotherapy directs attention to a specific ligament that has not been sufficiently strengthened and, used in conjunction with the trigger point of pain, should enable the physician to permanently cure the patient to his satisfaction.

Forty years' experience has strengthened the dictum of Stimson * that x-rays should never be examined until a provisional diagnosis has been arrived at following the history and physical examination.

* L. A. Stimson, Professor of Orthopedic Surgery, Cornell University Medical College, circa early 20th century.

Summary

Referred pain into the lower abdomen, groin, genitalia, buttock, and extremities to as far as the toes has its origin in the sensory nerves of ligaments supporting the lumbar and pelvic articulations.

Referred pain into the lower extremities is caused more often by ligament relaxation of the lumbar and pelvic articulations than from all other causes combined, in the experience of the author.

Pain and referred pain result when stretching of relaxed ligament fibers under normal tension induces an abnormal stimulation of the sensory nerves within the ligament, which will not stretch.

Over 90% of the undiagnosed chronic cases of low back disability, accompanied by referred pain into the extremities, are due to relaxation of the lumbar and pelvic articular ligaments.

A dermatome of referred pain into the lower abdomen, groin, genitalia, and extremities has been designed from observations while making over 6000 intraligamentous injections in 1017 cases during the past 17 years. It will endure as long as man walks upright.

Knowledge of the referred pain areas from specific ligaments enables the physician to identify more readily the particular joint ligament which is causing disability, and together with the available knowledge of muscle, bone, disc, spinal fluid, and spinal cord, with its nerves of distribution, will enable the physician to diagnose low back disability with confidence.

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Comment

This article has occasioned a good deal of discussion among the reviewing editors and consultants as to whether the author has fully supported his thesis in the material which he has presented. Certainly the material is controversial and will lead to discussion pro and con. Although their opinions varied, the editors decided to publish this paper, recognizing both its controversial nature and its merit. The editors will be glad to receive for publication in the A. M. A. Archives of Surgery letters from the readers of the article who are experienced in management of cases of this type giving their viewpoints.

Waltman Walters, M.D.

Editorials

A PROBLEM IN PALLIATION

DISTRESSING experiences with some of the more malignant types of cancer often cause surgeons to make unwarranted generalizations about the natural course of the disease. They may believe that unless a cancer can be eradicated, the patient is doomed to death. In such cases they assume that if a radical operation can be done the patient has everything to gain, and that if he dies as a result of treatment he has lost nothing. In the light of this philosophy any risk or any disability seems justified. But is it?

In the natural history of cancers, some grow very slowly, give few if any symptoms, and show little tendency to systemic dissemination, even over a period of years. These are the same cancers that usually are cured by radical surgery. Many of them are equally curable by simple eradication of the local lesion. Many of them, even if untreated, may not cause discomfort or death.

In young or middle-aged patients, if there is a reasonable chance of eradicating cancer, the most radical operation may be justified, for in these cases there is much to be gained in terms of extending the years of useful life. But in the aged, the situation is different. Here we are not concerned with the "saving of life" in the same sense that we can "save" or at least prolong for many years the life of a youth. In many such cases complete eradication of the cancer is less important than enabling the patient to live in comfort with his disease.

The death of an aged patient, whether he has cancer or not, is inevitable, and if it does not come from one cause it soon must come from another. In this age group we must view all of our patients as doomed to death and all of our operations as palliative. Our object is not to "save life" but to prolong it and to make the remaining years more pleasant and useful. Often this aim can be attained by treatments that are simple and safe and which, even in the young, are nearly as effective as standard radical treatment. Examples of this are cholecystoenterostomy for cancer of the pancreas; cholecystoenterostomy and transduodenal electrocoagulation of cancer of the ampulla of Vater; lobectomy for cancer of the lung; simple mastectomy for cancer of the breast; electrocoagulation of small, low-lying cancers of the rectum; electrocoagulation of cancers of the tongue and jaw; irradiation for cancers of the lip, larynx, and esophagus; diethylstilbestrol for cancers of the prostate, and symptomatic treatment for infiltrating cancers of the body or cardiac end of the stomach. Following all of these treatments the survival rate, even in younger people, is nearly as great as that following radical operations.

For most patients in the seventies and eighties the span of pleasant and useful life is destined to be so short that there is no advantage in risking immediate death or prolonged disability in order to obtain a little better chance of long-range cure. Viewed statistically, the days lost by the many aged patients who suffer death or disability following radical operations far outnumber the days that might be gained by the few whom only a radical operation could cure. Conservative measures are well adapted to the treatment of cancer in the aged and even with palliative treatment the length of comfortable life may be astonishingly long.

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Received for publication May 21, 1956.

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Case Reports

JUVENILE NASOPHARYNGEAL FIBROMA

Radical Surgical Approach

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and
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JUVENILE nasopharyngeal fibromas are rare lesions, histologically benign, but in some instances they produce clinical manifestations which justify radical surgical excision. Some, because of their small size, lack disturbing symptoms and pass into the "fibrotic burnt out" postadolescent stage almost unnoticed. At the other extreme are cases in which the tumor continues to grow and results in deformity in a young person. In this latter group are lesions which produce recurrent episodes of severe epistaxis and sepsis and fail to respond to conventional forms of radiological, hormonal, and surgical therapy.

The infrequent occurrence of this lesion is self-evident when one reviews the literature. The largest series is that of Figi and Davis, who reported 114 cases from the Mayo Clinic in 1950. Martin and coworkers reported 29 cases from the files of the Memorial Hospital, where some 2000 head and neck neoplasms are seen yearly, and, of these, 2 per year are juvenile fibromas. Shaheen reported 58 cases, but because of the older patients in this series some cannot be regarded as juvenile fibromas.

There are four clinical criteria which help make the diagnosis: 1. The tumor is polypoid and vascular, arises from the anterior superior wall of the nasopharynx, and enlarges slowly. 2. It has its onset during adolescence—average age 11 years. 3. The tumor has a high preponderance in the male sex, although Figi reports five cases and Ward and Hendricks report one case occurring in females. 4. The tumor has a tendency to spontaneous regression as sexual maturity is reached.

Grossly, these tumors are singular reddish polypoid structures which arise from the superior aspects of the nasopharyngeal vault. Their growth is slow but persistent and usually along lines of least resistance. The tumor may enter the posterior nasal choanae and may even present itself at the anterior nasal orifice. Continued enlargement in the confined space of the nasopharynx results in pressure necrosis of the adjacent bony structures and continued extension.

Growth into the maxillary sinus and cheek may occur. The tumor may erode into the orbit, causing exopthalmus and lateral displacement of the eye or the "frog face" described in the older literature (Fig. 1). The growth may erode through the hard palate and present as an intraoral submucosal tumor. No matter what the deformity is or the size of the tumor, its origin is always in the nasopharynx.

Obstruction of the nasopharynx produces the characteristic nasopharyngeal voice changes. A mucopurulent discharge may be present. The most frequent initial symptom is epistaxis. This is usually severe, may reach alarming proportions, and is extremely difficult to bring under control. The average history reports four or five such episodes

Submitted for publication April 18, 1956.

Roswell Park Memorial Institute; Associate Chief Cancer Research Head and Neck Surgeon (Dr. Marchetta); Associate Cancer Research Head and Neck Surgeons (Drs. Maxwell, Riegler, and von Schowingen).

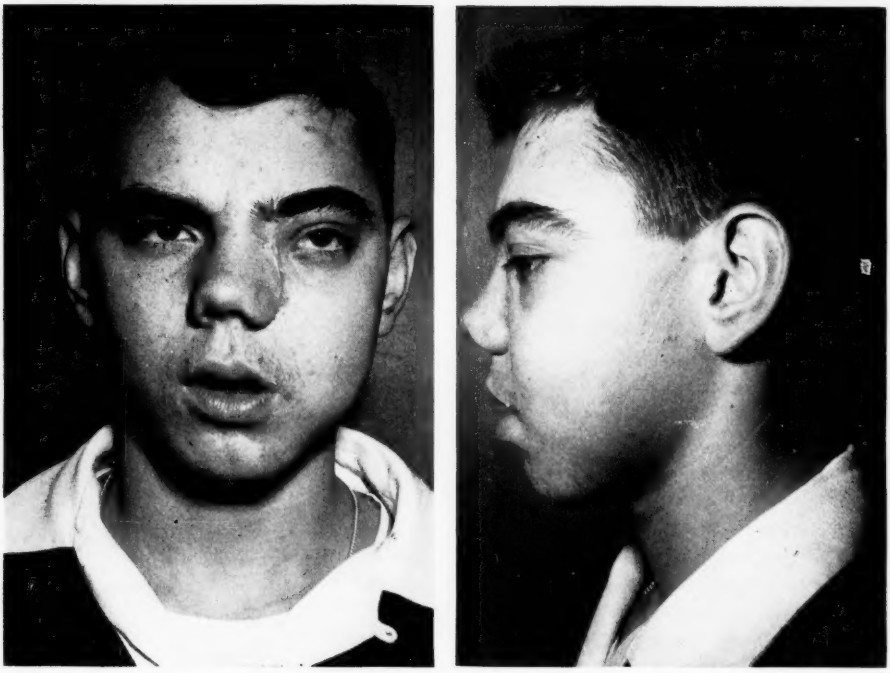

Fig. 1.—Appearance of patient (anteroposterior and lateral views) when first admitted to the Head and Neck Clinic, in 1953.

before the anatomically hidden tumor is discovered. Local necrosis of tumor and sepsis produce areas from which repeated hemorrhages occur.

Microscopically, the tumor is a very vascular structure composed of an admixture of blood vessels and fibrous tissue. In smaller lesions the main blood supply is through the stalk attachment in the roof of the nasopharynx. As the growth proceeds, the lesion may pick up secondary blood supply at sites of impingement, making removal a difficult and bloody procedure. During the actively growing stage of the lesion, which corresponds to the preadolescent years of the afflicted person, the relative amount of blood vessel element is usually considerable. In the postadolescent person the lesion is represented by greater and greater amounts of the fibrous element and gradual lessening of the vascular element. In lesions treated by radiation and hormonal therapy, the same changes can be observed.

Treatment is basically directed at keeping this benign tumor under control until the avascular regressive postadolescent stage is reached. For those lesions which remain small and relatively asymptomatic, no treatment other than close-interval examination of the nasopharynx is needed. In those persons, biological sexual maturity will result in a complete end-result. The lesions which continue to grow sometimes produce recurrent episodes of severe epistaxis. Unilateral or bilateral external carotid artery ligation may be life saving.

Radiation therapy, including radium, external irradiation, and radon seeds, is recommended by some with the hope of reducing the amount of the vascular element and promoting progressive fibrosis. When judiciously used, the desired effect is often achieved. The effect of radiation dosage on the germinal centers of the developing facial bones cannot be prognosticated. The use of radium and radon seeds is not en-

tirely safe because of the danger of radionecrosis of adjacent bone.

It is felt by some that hormone therapy will promote progressive fibrosis such as occurs in the postadolescent stage. There are some reports of a dramatic specific response from this form of therapy. Hormone administration, however, though originally considered a probable, highly specific, form of therapy, is becoming progressively less relied upon.

Surgery, though theoretically the best form of therapy, has its shortcomings because of the relative inaccessibility of the nasopharynx. The surgical approaches to the nasopharynx are somewhat radical, and, because this is a histologically benign tumor in a young person, surgical intervention is reserved for the complications such as epistaxis and beginning of facial deformity. The usual surgical approaches described for the removal of this tumor are as follows: 1. The tumor may be removed piecemeal through the nose. 2. The tumor may be approached through a lateral rhinotomy incision and the nose. 3. The tumor may be approached through a Weber-Ferguson incision and the anterior wall of the antrum. 4. The tumor may be approached through an incision splitting the soft palate.

In each instance, the exposure is inadequate, the operator is working in a deep hole bounded by bony walls, the blood supply to the tumor cannot be controlled at its source, and bleeding is profuse. Complete removal is, in most instances, impossible.

There is still another approach, described by A. J. Kremen in 1953, which provides adequate exposure, permits ligation of the vessels supplying the tumor at their origin, and insures complete removal of the tumor. The following is a case report which illustrates some of the manifestations of this tumor and radical excision as described by A. J. Kremen.

The patient sustained his first episode of epistaxis after trivial trauma in September, 1951. The family physician experienced considerable difficulty in controlling the hemorrhage. In the next six months there were six more bouts of left-sided epistaxis. During this period the family noted a gradually developing nasal voice change and left-sided facial asymmetry. He was referred to a neighboring medical center, and nasopharyngeal examination revealed a reddish polypoid tumor in the left nasopharynx which had grown through the left posterior choanae and could be visualized in the nasal cavity by speculum examination. Biopsy showed this to be a "juvenile nasopharyngeal fibroma."

In January, 1952, operation was performed. The tumor was approached thru a combined Killian and Caldwell-Luc incision, and excision was considered adequate. Ten months later, however, recurrence was noted. The tumor was partially removed through the nasal cavity. Rapid regrowth occurred, and this was followed by two subsequent hospitalizations, and electrocoagulation of the tumor through the nose was performed to control its growth. At this time, 18 months after the first treatment for his condition, the patient was referred to the Roswell Park Memorial Institute.

The patient was admitted to the Head and Neck Department in September, 1953. Physical examination revealed a well-developed well-nourished 15-year-old youth. There was asymmetry of the left side of the face. The left eye showed some degree of proptosis and lateral displacement. There was a well-healed scar along the left side of the nose. A reddish polypoid tumor was visualized in the nasopharynx, and the mass was also visualized by speculum examination of the nose. Repeat biopsy showed a "nasopharyngeal fibroma."

Surgical removal was attempted, this time through a Weber-Ferguson incision. The tumor was removed from the nose and the maxillary antrum, and some was removed from the nasopharynx. In spite of external carotid artery ligation, hemorrhage was profuse, and the operation was terminated. Two weeks later, the nubbin of remaining tumor was seeded with four (1 mc.) radon seeds.

In June, 1954, the patient was again admitted because of progressive nodular enlargement in the substance of the left cheek. This mass extended posteriorly into the pterygomaxillary space. The tumor was removed thru an intraoral approach.

The patient was again seen in October, 1955. His speech was nasal in character. He had experienced several nose-bleeds, one of which required several transfusions for control. There was a mucopurulent discharge from the left nostril and nasopharynx. The tumor had grown downward, causing a bulge of considerable size in the left soft palate. The severe hemorrhages provided the main indication for surgery, and the tumor was excised with use of a lateral approach thru the cheek and mandible.

Fig. 2.—Skin incision for lateral approach to nasopharynx.

Fig. 3.—Transection of the ascending ramus of mandible.

Fig. 4.—Nasopharyngeal tumor exposed.

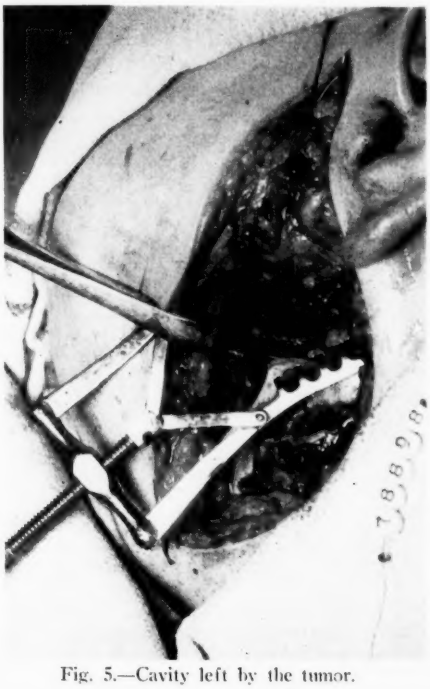

Fig. 5.—Cavity left by the tumor.

Fig. 6.—Operative specimen.

The skin incision began in the crease anterior to the ear, extended downward behind the angle of the jaw, and curved on to the neck to run parallel to the inferior border of the mandible (Fig. 2). The incision was carried down through the subcutaneous fat tissue through the platysma muscle. Anterior and posterior flaps were developed in this tissue plane. The mandibular branch of the facial nerve was identified. The masseter muscle was exposed in this area, sparing the branches of the nerve. The masseter muscle was transected approximately 1.5 cm. above its insertion on the mandible. A periosteal elevator was used to dissect the muscle and overlying tissues away from the mandible. The ascending ramus of the mandible was transected with a Gigli saw (Fig. 3). The cut ends of the mandible were separated with a self-retaining mastoid retractor, and the pterygoid muscle was retracted medially. This exposed the tumor (Fig. 4). By means of blunt and sharp dissection, the tumor was gradually delivered. Bleeding was not a problem. The cavity left by the tumor is shown in Figure 5. In this photo, one can identify the parotid gland anterior to the lobule of the ear. The facial nerve remained intact. The cut ends of the man-

dible were approximated with No. 25 dental wire, and the remaining tissues were closed in layers. The operative specimen is shown in Figure 6.

The postoperative course was without incident. The mandible showed good union. There has been no evidence of recurrence.

Summary

The clinical manifestations of juvenile nasopharyngeal fibroma are reviewed. Juvenile nasopharyngeal fibromas, though histologically benign tumors, sometimes require surgery of a radical nature to excise them. Recurrent episodes of severe epistaxis and beginning of facial deformity are indications for radical approach to the tumor. The operation is a logical one and can be performed without permanent disability.

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FIBROSARCOMA OF THE KIDNEY

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and
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FIBROSARCOMA of the kidney is an interesting and perplexing tumor. It has no respect for age, nor does it affect one side or one sex more commonly than the other. The presence of a mass in the flank is, as with most renal neoplasms, an important sign. More than 80% of all cases in the literature manifested themselves first as a flank mass. Pain was the next commonest finding, but there were cases in which the fibrosarcoma was a silent, painless tumor. Hematuria was, unfortunately, a late and inconstant finding. The constitutional symptoms of weight loss, malaise, anorexia, and anemia were legion in this group of patients.* We have recently seen a primary fibrosarcoma of the kidney in a 69-year-old woman and were stimulated to review the literature and to consider the pathogenesis, prognosis, and therapy of renal fibrosarcomas.

Fig. 1.—Pyelogram showing mass lesion at the lower pole of the left kidney and probable cyst of the right kidney.

Fig. 2.—Aortogram, demonstrating vascularity of lesion on left side as compared with translucent mass on the right.

Report of Case

A 69-year-old woman was admitted to the University Hospital because of postmenopausal bleeding. Studies revealed microscopic hematuria and

Submitted for publication May 21, 1956.

From the Department of Surgery, Division of Urology, Hospital of the University of Pennsylvania.

* References 2-6.

a palpable left upper quadrant mass. Hemoglobin determination was recorded as 8.6 gm. per 100 cc. Pyelograms revealed a mass lesion in the left kidney and a right renal cyst (Fig. 1). Roentgen examination of the chest was within normal limits. An aortogram revealed a right renal cyst and was highly suggestive of tumor on the left (Fig. 2).

The left retroperitoneal space was explored, and biopsy of the left kidney showed a neoplasm of unknown type, probably malignant. Following this, a left nephrectomy was performed.

The kidney weighed 680 gm., and sections showed a firm pinkish tumor replacing the lower pole. Several cysts were noted, (Figs. 3 and 4). Microscopically the tumor was composed of interlacing strands of fibrous tissue. Some areas showed much collagenous fibrous tissue stroma with few cells. Mitoses were rare (Fig. 5). A pathological diagnosis of fibrosarcoma of the kidney was made. Since nephrectomy, the patient has had a right nephrostomy and intubated ureterostomy, with removal of a large cyst of the lower pole. This was, microscopically, a retention type of cyst, and not malignant. The patient has had an uneventful recovery and is well at this time—18 months postoperatively.

Fig. 3.—Gross specimen of left kidney tumor mass replaces lower two-thirds of organ.

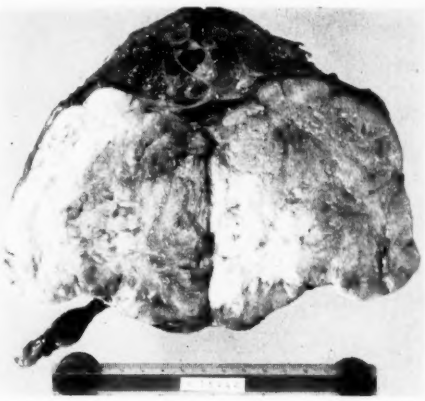

Fig. 4.—Gross specimen sectioned, showing fibrous appearance of tumor.

Comment

Fibrosarcoma is the name given to malignant neoplasia of fibroblasts. The literature is replete with the terms fibromyxosarcoma, fibrochondrosarcoma, and round-cell and spindle-cell sarcoma. It is important to recognize the fibroblast as an omnipotential cell, one which may dedifferentiate into myxoid or cartilagenous forms. Moreover, a spindle-shaped fibroblast when sectioned transversely to its long axis appears as a round cell, and the converse obviously obtains. Recent tissue culture and tissue transplant work indicates that the simple histogenetic approach to the taxonomy of these tumors is the most valid.[1] As both Mintz [2] and Judd [3] point out, many of the previously reported renal fibrosarcomas need to be reevaluated in light of modern pathology and histogenetic nomenclature.

A study from the Mayo Clinic showed the incidence of fibrosarcoma to be 1:30,300 admissions.[3] During the period 1904-1940, there were 35 cases of fibrosarcoma of the kidney reported at that institution. Mintz [2] reviewed 96 cases of renal sarcoma and found 12 that could be classified as true fibrosarcoma. In another series of 570 cases operated on for renal tumor, 6 were found to be fibrosarcoma.[4] Moore [5] and Ruff [6] have added two additional cases from their own experience, and one case of bilateral renal fibrosarcoma has been reported.[2]

Microscopically, the tumor is composed of spindle-shaped fibroblasts and connective tissue fibers. Reticulin fibers are always present. The relationship of fibroblasts to reticulin and collagen fibers is important in separating fibrosarcomas into two cate-

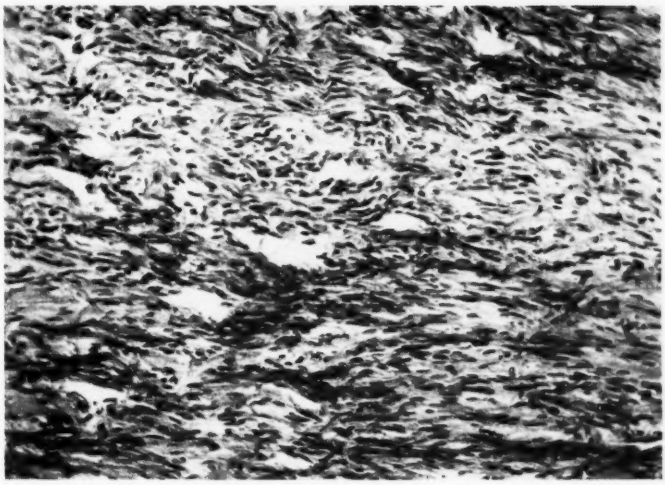

Fig. 5. — Microscopic appearance of tumor fibrosarcoma.

gories. The majority are well differentiated and have delicately interlacing patterns of fibrils and cells that are mature and show few, if any, mitoses. In the less-well-differentiated forms, the fibrils predominate and cells are closer together, with hyperchromatic nuclei and frequent mitoses. This is an important distinction to make, from a prognostic point of view. In Stout's series of well-differentiated fibrosarcomas [7] there were no distant metastases, although the recurrence rate was 42%. Only 3.8% of this group died as a direct consequence of the tumor. In the group with poorly differentiated fibrosarcomas, 24% had distant metastases and 50% died as a result of the tumor.[8]

The life history of a fibrosarcoma is unpredictable and probably represents varying degrees of tumor autonomy. Serial sections of any fibrosarcoma may show areas of intense activity in close association with areas of relative inactivity.[8] Clinically, the tumor may have spurts of growth and then enter a period of relative dormancy for months or even years. The microscopic pattern of the tumor lends support to the clinical impression that infiltration well beyond the palpable and grossly visible aspects of the tumor are to be expected. It is for this reason that wide excision, with generous margins of the adjacent tissue, is to be recommended.

While fibrosarcoma is primarily a tumor of skin, subcutaneous tissues, scars, etc., it is a tumor which urologic surgeons should be familiar with from the standpoint of pathogenesis, prognosis, and therapy.

Summary

A case of primary fibrosarcoma of the kidney is presented. The essential pathologic and clinical features are discussed.

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SARCOMA OF THE PANCREAS

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and
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SARCOMA of the pancreas is comparatively rare. We have found records of 203 cases of sarcoma or carcinosarcoma observed at autopsy.* However, only three cases have been reported which were successfully treated by radical pancreaticoduodenectomy.†

Our case is reported because of its rarity, the difficulty encountered in establishing an accurate diagnosis by frozen section biopsy, and the excellent progress of the patient after one year.

Report of Case

A 47-year-old accountant was admitted to the Methodist Hospital on Jan. 10, 1955. He had noticed generalized itching for about one month and diarrhea for two weeks. The stools were acholic. Jaundice became apparent about 12 days before admission to the hospital, but there was no pain. Weight loss was 12 lb. in 30 days.

In 1933 and again in 1954 the patient passed small renal calculi, without apparent kidney damage. In 1946, diabetes was discovered and readily controlled by diet. The blood sugar during these years averaged about 150 mg. per 100 cc.

The patient had received chlorpromazine (Thorazine) hydrochloride to control itching, and it was thought that the jaundice might have been due to the use of this drug. However, the jaundice and itching persisted after all drugs had been discontinued. The stools became brown on one occasion and remained so for a few days but soon resumed their clay-colored appearance. The patient had been exposed to carbon tetrachloride fumes six to eight months previously, while exterminating rodents in a bin of rye. Moreover, three or four days before the onset of jaundice, he extinguished a fire in his machine shop with carbon tetrachloride. Therefore, the possibility of this cellulotoxic agent as a causative factor was considered.

We saw the patient three weeks after admission to the hospital. The enlarged liver, which had been noted previously, had increased in size and had become bosselated. The gall bladder was greatly enlarged. All laboratory findings were within average limits except the serum bilirubin, which was elevated, showing 13.4 mg. per 100 cc. as a direct reaction and 12.2 mg. as indirect. The fasting blood sugar was 185 mg. per 100 cc., but the urinalysis was normal except for bile. Repeated tests showed normal urinary diastase, serum calcium, serum alkaline phosphatase, and coagulation time. There was no steatorrhea or creatorrhea despite the absence of bile in the stools. X-ray studies of the chest and gastrointestinal tract disclosed no abnormalities.

Our preoperative diagnosis was obstructive jaundice due to carcinoma of the pancreas, with metastases to the left lobe of the liver.

Operative Procedure

On Feb. 23, 1955, abdominal exploration was done, under general anesthesia. The gall bladder was distended greatly, measuring 10×14 cm. Likewise, the cystic and common ducts were enormously dilated. The liver extended to about 12.5 cm. below the right costal margin and 8 cm. below the xiphoid. Its surface was smooth, without evidence of metastases. A hard tumor could be felt in the head of the pancreas, which appeared to be about 5.5 cm. in diameter. Exploration of the remainder of the peritoneal cavity revealed no gross evidence of neoplasia.

Biopsy from the pancreas showed what was thought to be fibroadenoma, and lymph nodes were normal. The lesion was definitely invasive on gross examination, and therefore we decided to remove it with a wide margin of normal tissue. The common bile duct was divided distal to the cystic duct, and a radical pancreaticoduodenectomy was done, with removal of approximately one-half of the pancreas and the entire duodenum. One thousand cubic centimeters of whole blood and one thousand cubic centimeters of isotonic saline were given during the operation, which required about six hours. The patient tolerated the procedure well.

The postoperative course was without complications except for the diabetes. Blood sugar values rose rapidly following surgery, reaching 262 mg. on the ninth postoperative day. This was easily

Received for publication March 27, 1956.

From the Departments of Surgery, Methodist Hospital, and the Indiana University Medical Center.

* References 2 and 6-9. Oberling and Guerin, quoted in Reference 5.

† References 1, 3, and 4.

A, photomicrograph of representative area through the sarcoma, showing spindle-shaped cells in atypical arrangement; reduced ¼ from mag. × 100. *B*, higher power of the section shown in (*A*). Note the giant-sized cells with greatly enlarged and distorted nuclei. The cytoplasm is eosinophilic; reduced ¼ from mag. × 350.

controlled with insulin, and the patient is now receiving 20 units of lente insulin per day. When last seen, on Feb. 27, 1956, he had gained 40 lb. in weight and was entirely free of symptoms.

Comment

Frozen sections are sometimes difficult to interpret in pancreatic disease, and the impression in this case was fibroadenoma. However, the lesion was grossly invasive, and therefore radical pancreaticoduodenectomy was carried out. Permanent sections were interpreted as sarcoma, probably of smooth-muscle origin, which had invaded the ampullary region and the common bile duct (Figure).

Summary

A patient with sarcoma of the pancreas was treated by radical pancreaticoduodenectomy. There was no evidence of recurrence after one year.

Addendum

One year and seven months (Sept. 6th) after operation a complete examination failed to reveal any signs of recurrence.

Weight has remained about the same, with a slight increase when reducing diet is not observed.

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Surgery Illustrated

A SURGICAL MANEUVER FOR EXPOSURE OF THE VESSELS OF THE SUPERIOR POLE DURING THYROIDECTOMY

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Illustrations by Mary Maciel

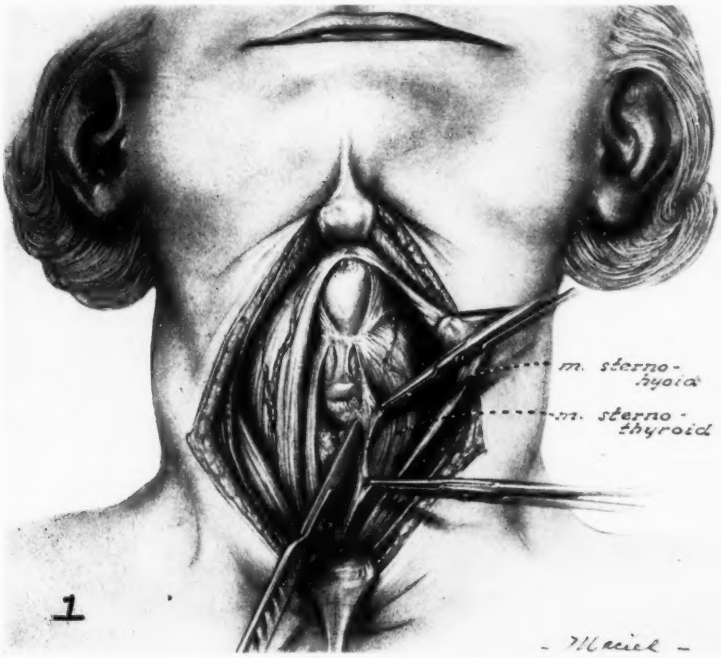
THE USUAL Kocher collar incision is made, and the superior and inferior flaps expose the deep cervical fascia from the thyroid cartilage of the larynx to the suprasternal notch. The sternohyoid and sternothyroid muscles are reflected laterally and individually from the midline to the neurovascular bundle (Fig. 1). The superior portion of the sternohyoid muscle is retracted, exposing the insertion of the sternothyroid muscle (Fig. 2). By careful sharp and blunt dissection the sternothyroid muscle is reflected over most of the superior pole. The posterior lateral edge of this muscle is freed of areolar tissue, and the common carotid artery and internal jugular vein are mobilized posteriorly (Fig. 3).

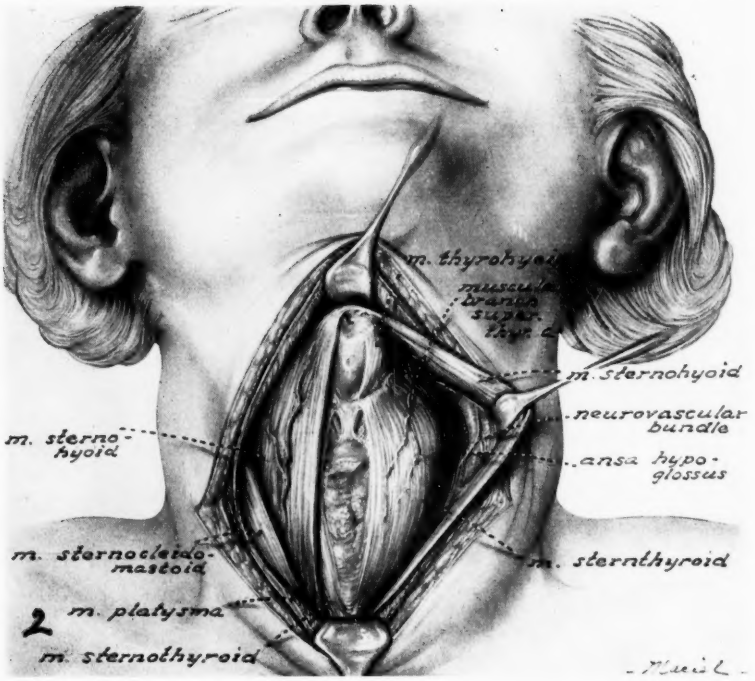
With care, the musculotendinous insertion of the sternothyroid muscle is completely cut, thus exposing the entire superior pole of the thyroid gland including its vessels. This obviates the necessity of cutting the sternohyoid and sternothyroid muscles in their midportion, which actually does not aid exposure of the superior pole, particularly in extremely large goiters (Fig. 4).

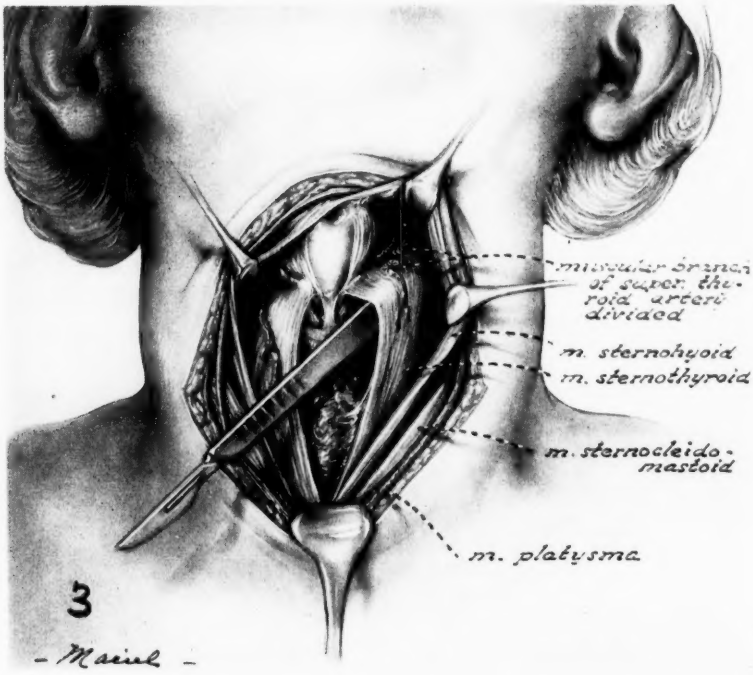
The superior medial border of each sternothyroid muscle is approximated to the midline, returning the muscles to a normal position covering the resected area of the remaining gland. The structures are closed in layers with inverted interrupted 0000 nonabsorbable surgical (silk) sutures (Fig. 5).

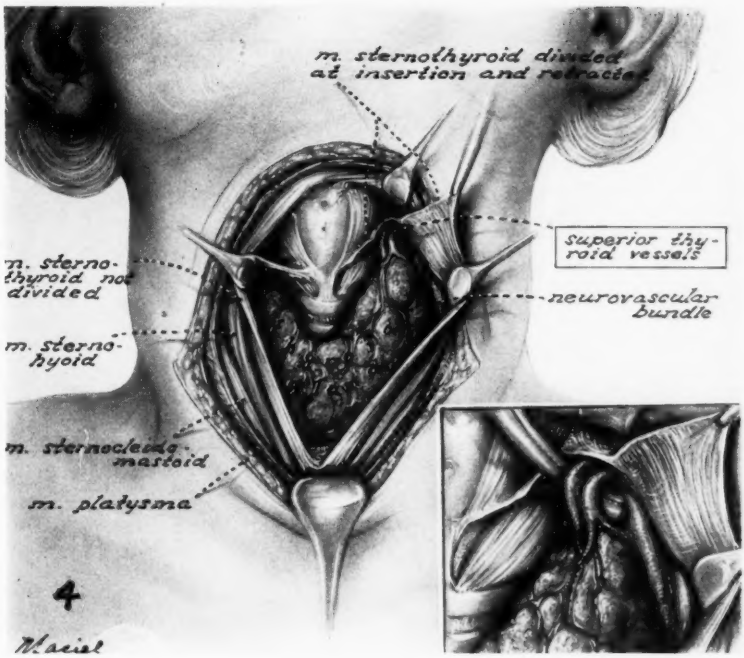
Recorded for publication July 19, 1956.

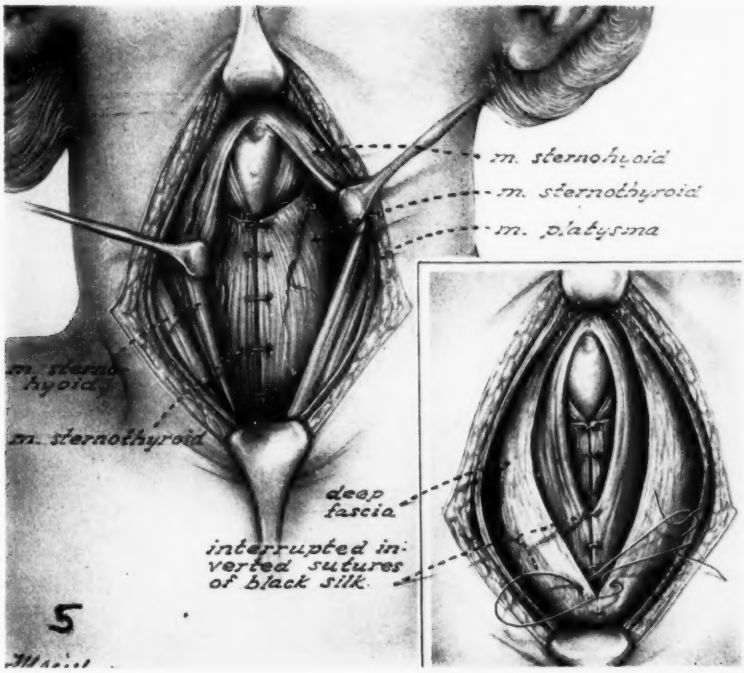
From the Department of Surgery, College of Medicine, University of Cincinnati.




m. thyrohyoid
muscular branch super. thyr. a.
m. sternohyoid
neurovascular bundle
ansa hypoglossus
m. sternohyoid
m. sternocleidomastoid
m. sternothyroid
2
m. platysma
m. sternothyroid
- Maisel -


muscular branch of superior thyroid artery divided
m. sternohyoid
m. sternothyroid
m. sternocleidomastoid
m. platysma
3
- Maisel -


m. sternothyroid divided at insertion and retracted
superior thyroid vessels
m. sternothyroid not divided
neurovascular bundle
m. sternohyoid
m. sternocleido-mastoid
m. platysma
4
Macial


m. sternohyoid
m. sternothyroid
m. platysma
m. sternohyoid
m. sternothyroid
deep fascia
interrupted inverted sutures of black silk
5

Correspondence

AXILLARY CYSTIC HYGROMA

To the Editor:—I note with interest the article on cystic hygroma of the axilla in the A. M. A. Archives of Surgery, Volume 72, page 824, May, 1956. Until seeing this, I had not realized the extreme rarity of this lesion, which prompts me to make the following report to you.

In January, 1956, I saw a similar tumor mass in the right axilla of a one-year-old child. The mother stated that a small lump about 2 in. in diameter had been present in the axilla adjacent to the chest since the age of 4 months. This lump was unchanged until approximately the first of January, 1956, at which time, over the course of about two weeks, rapid enlargement occurred, until the mass attained the size of about 10 in. in diameter.

My clinical diagnosis was cystic hygroma. The child was operated upon on Feb. 10, 1956, and a copy of the operative and pathological reports is submitted.

Operative Report

Operation (Dr. Kridelbaugh and Dr. Gordon).—Excision of hygroma, right axilla.

Procedure.—An elliptical incision was made, excising a small piece of skin, the incision being placed transversely across the tumor mass. The superior flap was dissected up to the clavicle, the inferior flap down to the base of the latissimus dorsi muscle. The tumor mass was then freed by freeing the lower margin and working around through the subcapsular fossi and then working medially and superiorly until we had reached and identified the axillary vein, which was surrounded by the cystic hygroma. With some difficulty it was dissected free from this structure, following which we found that it extended upwards posterior to the axillary artery and brachial plexus, reaching the base of the neck above the clavicle. With some difficulty this was dissected out, taking care to remove all lobules of the tumor. After completion of the procedure, a Penrose drain was placed in the wound and brought out through a stab wound inferior to the incision. The incision was closed with subcutaneous sutures of plain 000 and skin sutures of 000 silk. The patient withstood the procedure well, receiving 200 cc. of blood during the operation, and returned to the recovery room in good condition.

Pathology Report

Gross Description (Dr. V. H. Beighley).—The specimen consists of a tumor from the right axilla. This specimen measures approximately 8.5 cm. in diameter. It is lobulated and cystic; one surface is covered with an elliptical portion of skin measuring 7 cm. in length and 1 cm. in greatest width. Cut section of the tumor shows it to be extremely cystic. The cysts are filled with a bloody material, some of which is brown.

Microscopic Description.—Sections show many cystic spaces which appear to be lined by a flattened layer of endothelium, and the wall contains a connective tissue which is extremely edematous and shows a focal infiltration with lymphocytes. There is no evidence of malignancy.

Diagnosis.—Lymphangioma (cystic hygroma) from the right axilla.

At the present time the patient shows no sign of recurrent tumor.

W. W. Kridelbaugh, M.D., Albuquerque, N. M.